

NMCP COVID-19 Literature Report #78: Friday, 08 October 2021

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Purpose: These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at <https://nmcp.libguides.com/covidreport>. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

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The Big Picture

News in Brief

Francis Collins, who served as Director of the National Institutes of Health for more than 12 years, is stepping down by the end of the year ([NIH](#)).

"COVID spike pushes Alaska's health care system to brink" ([AP](#)).

"Experts weigh in on when the public health emergency should end" ([WP](#)).

"Will the pandemic fade into an ordinary disease like the flu? The world is watching Denmark for clues" ([Science](#)).

Supply Chain Issues

Remember early in the pandemic there was a shortage of toilet paper, [among other things](#)? It's soon likely to be worse: "Here is an incomplete list of consumer goods that have been subject to backorders, delays, and shortages: [new clothes](#), [back-to-school supplies](#), [bicycles](#), [pet food](#), [paint](#), [furniture](#), [cars](#), [tech gadgets](#), [children's toys](#), [home appliances](#), [lumber](#), [anything that relies on semiconductor chips](#), and even coveted fast food staples like [chicken wings](#), [ketchup packets](#), [Taco Bell](#), [Starbucks' cake pops](#), and [McDonald's milkshakes](#) (in the UK, for now)." ([Vox](#); see also: this Vox article on a [book shortage](#)).

The DOD isn't having a great time with supply chain issues, either - especially with pharmaceuticals ([CIDRAP](#); see also: [IG report with redactions \[pdf\]](#)).

Preparedness

"House votes to create office for medical intelligence to get earlier pandemic warnings — A provision inserted into a bill approved by the House Intelligence Committee would create authorities to counter foreign biological threats" ([NBC](#)).

"Before the pandemic, the United States had begun building a special pathogen system. What can we learn from its COVID-19 response?" ([Health Affairs](#)).

Long Reads

"We're already barreling toward the next pandemic — This one is far from over, but the window to prepare for future threats is closing fast" ([Atlantic](#)).

"Messy, incomplete U.S. data hobbles pandemic response — The nation's decentralized, underfunded reporting system hampers efforts to combat the coronavirus" ([WP](#)).

"20 years after the anthrax attacks, we're still unprepared. The first fatal bioterror attack in the US killed five people and caused a national panic—and we're still short of funding and tech to handle health emergencies" ([Wired](#)).

Special Reports and Other Resources

DOD: [Department of Defense Climate Adaptation Plan \[pdf\]](#) (01 September 2021)

Statement by Secretary of Defense Lloyd J. Austin III:

"Climate change is an existential threat to our nation's security, and the Department of Defense must act swiftly and boldly to take on this challenge and prepare for damage that cannot be avoided. Every day, our forces contend with the grave and growing consequences of climate change, from hurricanes and wildfires that inflict costly harm on U.S. installations and constrain our ability to train and operate, to dangerous heat, drought, and floods that can trigger crises and instability around the world.

The Climate Adaptation Plan will be our guide for meeting the nation's warfighting needs under increasingly extreme environmental conditions—and for maintaining force readiness and resilience well into the future.

This plan will help the Department of Defense integrate climate considerations into our operations, our planning, and our business and decision-making processes. That includes how we train and equip our forces and new measures to strengthen the resilience of our infrastructure. This plan will also help ensure that our supply chains adapt to the realities of our changing climate.

We must take on these challenges as a team—from every corner of the Pentagon, on each of our installations and bases, across the federal government, and alongside our partners and allies.

We do not intend merely to adapt to the devastation of climate change. We will work with nations around the world to meet the threat. Tackling these challenges also presents an opportunity, because the bold steps we are taking are good for the climate and also good for our mission of defending the nation. With this roadmap, the U.S. military will become even more resilient, efficient, and innovative—and remain the world's preeminent fighting force, ready to confront the risks of today and tomorrow."

CNS: [OP #52: Scientific Risk Assessment of Genetic Weapons Systems](#) (23 September 2021)

"For any emerging technology, defense and homeland security analysts strive to understand (1) its dual-use potential, meaning whether the same research and technology applied for peaceful purposes may be diverted to illicit ends, for example to develop a weapon; (2) the State and sub-State actors with access to that dual-use potential, whether peacefully or illicitly directed; and (3) motivational factors and indicators of intent that might suggest these actors would divert the emerging technology to illicit ends. Precision medicine represents one such emerging technical space. Precision medicine is defined as medical care designed to optimize benefit for particular groups, especially based on genetic (or

molecular) profiling. A long-speculated but incompletely understood dual-use consideration of precision medicine is the possible development of a genetic weapon system, defined as a weapon system designed to optimize effect on particular groups based on genetic profiling.

This Occasional Paper assesses the potential for precision medicine to be diverted to develop a population-specific genetic weapon system, examines relevant state capabilities and motivations to pursue such an effort, and offers policy recommendations to manage the dual-use implications of this emerging biomedical field while still preserving its potential benefit for human welfare."

See also: [webinar](#) that discusses overview of topic

Journal Articles

Int J Epidemiol: [Quantifying impacts of the COVID-19 pandemic through life-expectancy losses: a population-level study of 29 countries](#) (26 September 2021)

"Background: Variations in the age patterns and magnitudes of excess deaths, as well as differences in population sizes and age structures, make cross-national comparisons of the cumulative mortality impacts of the COVID-19 pandemic challenging. Life expectancy is a widely used indicator that provides a clear and cross-nationally comparable picture of the population-level impacts of the pandemic on mortality.

Methods: Life tables by sex were calculated for 29 countries, including most European countries, Chile and the USA, for 2015-2020. Life expectancy at birth and at age 60 years for 2020 were contextualized against recent trends between 2015 and 2019. Using decomposition techniques, we examined which specific age groups contributed to reductions in life expectancy in 2020 and to what extent reductions were attributable to official COVID-19 deaths.

Results: Life expectancy at birth declined from 2019 to 2020 in 27 out of 29 countries. Males in the USA and Lithuania experienced the largest losses in life expectancy at birth during 2020 (2.2 and 1.7 years, respectively), but reductions of more than an entire year were documented in 11 countries for males and 8 among females. Reductions were mostly attributable to increased mortality above age 60 years and to official COVID-19 deaths.

Conclusions: The COVID-19 pandemic triggered significant mortality increases in 2020 of a magnitude not witnessed since World War II in Western Europe or the breakup of the Soviet Union in Eastern Europe. Females from 15 countries and males from 10 ended up with lower life expectancy at birth in 2020 than in 2015."

Eur J Clin Invest: [Noncommunicable diseases, climate change and iniquities: What COVID-19 has taught us about syndemic](#) (22 September 2021)

"Background: COVID-19 is generating clinical challenges, lifestyle changes, economic consequences. The pandemic imposes to familiarize with concepts as prevention, vulnerability and resilience.

Methods: We analysed and reviewed the most relevant papers in the MEDLINE database on syndemic, noncommunicable diseases, pandemic, climate changes, pollution, resilience, vulnerability, health costs, COVID-19.

Results: We discuss that comprehensive strategies must face multifactorial consequences since the pandemic becomes syndemic due to interactions with noncommunicable diseases, climate changes and iniquities. The lockdown experience, on the other hand, demonstrates that it is rapidly possible to reverse epidemiologic trends and to reduce pollution. The worst outcome is evident in eight highly industrialized nations, where 12% of the world population experienced about one-third of all COVID-19-deaths worldwide. Thus, a great economic power has not been fully protective, and a change of policy is obviously needed to avoid irreversible consequences.

Conclusions: We are accumulating unhealthy populations living in unhealthy environments and generating unhealthy offspring. The winning policy should tackle structural inequities through a syndemic approach, to protect vulnerable populations from present and future harms."

Ann Intern Med: [Measuring the COVID-19 Mortality Burden in the United States](#) (21 September 2021)

"Background: Fully assessing the mortality burden of the COVID-19 pandemic requires measuring years of life lost (YLLs) and accounting for quality-of-life differences.

Results of base-case analysis: The COVID-19 pandemic resulted in 6.62 million QALYs lost (9.08 million YLLs) through 13 March 2021, with 3.6 million (54%) lost by those aged 25 to 64 years. The greatest toll was on Black and Hispanic communities, especially among men aged 65 years or older, who lost 1138 and 1371 QALYs, respectively, per 10 000 persons. Absent the pandemic, 38% of decedents would have had average or above-average life expectancies for their subgroup defined by age, sex, and race/ethnicity.

Conclusion: Beyond excess deaths alone, the COVID-19 pandemic imposed a greater life expectancy burden on persons aged 25 to 64 years, including those with average or above-average life expectancies, and a disproportionate burden on Black and Hispanic communities."

SARS-CoV-2 Virus and Variants

News in Brief

"COVID vaccines cut the risk of transmitting Delta — but not for long. People who receive two COVID-19 jabs and later contract the Delta variant are less likely to infect their close contacts than are unvaccinated people with Delta" ([Nature](#); see also: [medRxiv preprint](#)).

The USDA has confirmed a case of SARS-CoV-2 in a pet ferret in Florida; it is suspected that the ferret got the infection from a COVID-19 positive person ([USDA](#)).

Journal Articles

MMWR: [Distribution of SARS-CoV-2 Variants in a Large Integrated Health Care System — California, March–July 2021](#) (08 October 2021)

"What is already known about this topic? The highly transmissible SARS-CoV-2 (B.1.617.2) Delta variant is the predominant variant circulating in the United States.

What is added by this report? During March 4–July 21, 2021, sequencing data from 6,798 SARS-CoV-2–positive specimens were linked to electronic health records among Kaiser Permanente Southern California members. The weekly percentage of all infections attributed to the Delta variant rapidly increased to 95% during this period. Infection with the Delta variant was more common among younger persons and among non-Hispanic Black persons.

What are the implications for public health practice? These findings reinforce the importance of continued monitoring of SARS-CoV-2 variants and implementing multicomponent COVID-19 prevention strategies, particularly during the current period in which Delta is the predominant circulating variant in the United States."

Clin Infect Dis: [One-year sustained cellular and humoral immunities of COVID-19 convalescents](#) (05 October 2021)

"Background: The longitudinal antigen-specific immunity in COVID-19 convalescents is crucial for long-term protection upon individual re-exposure to SARS-CoV-2, and even more pivotal for ultimately achieving population-level immunity. To better understand the features of immune memory in individuals with different disease severities at one year post-disease onset we conducted this cohort study.

Methods: We conducted a systematic antigen-specific immune evaluation in 101 COVID-19 convalescents, who had asymptomatic, mild, moderate, or severe disease, through two visits at months 6 and 12 post-disease onset. The SARS-CoV-2-specific antibodies, comprising NAb, IgG, and IgM, were assessed by mutually corroborated assays, i.e.

neutralization, enzyme-linked immunosorbent assay (ELISA), and microparticle chemiluminescence immunoassay (MCLIA). Meanwhile, the T-cell memory against SARS-CoV-2 spike, membrane and nucleocapsid proteins was tested through enzyme-linked immunospot assay (ELISpot), intracellular cytokine staining (ICS), and tetramer staining-based flow cytometry, respectively.

Results: SARS-CoV-2-specific IgG antibodies, and also NAb can persist among over 95% COVID-19 convalescents from 6 months to 12 months after disease onset. At least 19/71 (26%) of COVID-19 convalescents (double positive in ELISA and MCLIA) had detectable circulating IgM antibody against SARS-CoV-2 at 12m post-disease onset. Notably, the percentages of convalescents with positive SARS-CoV-2-specific T-cell responses (at least one of the SARS-CoV-2 antigen S1, S2, M and N protein) were 71/76 (93%) and 67/73 (92%) at 6m and 12m, respectively. Furthermore, both antibody and T-cell memory levels of the convalescents were positively associated with their disease severity.

Conclusions: SARS-CoV-2-specific cellular and humoral immunities are durable at least until one year after disease onset."

CMAJ: [Evaluation of the relative virulence of novel SARS-CoV-2 variants: a retrospective cohort study in Ontario, Canada](#) (04 October 2021)

"Background: Between February and June 2021, the initial wild-type strains of SARS-CoV-2 were supplanted in Ontario, Canada, by new variants of concern (VOCs), first those with the N501Y mutation (i.e., Alpha/B.1.1.17, Beta/B.1.351 and Gamma/P.1 variants) and then the Delta/B.1.617 variant. The increased transmissibility of these VOCs has been documented, but knowledge about their virulence is limited. We used Ontario's COVID-19 case data to evaluate the virulence of these VOCs compared with non-VOC SARS-CoV-2 strains, as measured by risk of hospitalization, intensive care unit (ICU) admission and death.

Methods: We created a retrospective cohort of people in Ontario who tested positive for SARS-CoV-2 and were screened for VOCs, with dates of test report between Feb. 7 and June 27, 2021. We constructed mixed-effect logistic regression models with hospitalization, ICU admission and death as outcome variables. We adjusted models for age, sex, time, vaccination status, comorbid-ities and pregnancy status. We included health units as random intercepts.

Results: Our cohort included 212 326 people. Compared with non-VOC SARS-CoV-2 strains, the adjusted elevation in risk associated with N501Y-positive variants was 52% (95% confidence interval [CI] 42%–63%) for hospitalization, 89% (95% CI 67%–117%) for ICU admission and 51% (95% CI 30%–78%) for death. Increased risk with the Delta variant was more pronounced at 108% (95% CI 78%–140%) for hospitalization, 235% (95% CI 160%–331%) for ICU admission and 133% (95% CI 54%–231%) for death.

Interpretation: The increasing virulence of SARS-CoV-2 VOCs will lead to a considerably larger, and more deadly, pandemic than would have occurred in the absence of the emergence of VOCs."

COVID-19 Vaccines

News in Brief

"Pfizer, BioNTech ask FDA to authorize coronavirus vaccine for children 5 to 11 — An estimated 28 million children would be eligible for the shots in the United States if regulators give the green light" ([WP](#)).

"Lots of people say they'll quit over vaccine mandates, but research shows few do" ([NPR](#)).

"New U.S. travel rules close door on those fully vaccinated with Russia's Sputnik V" ([WP](#)).

"New HHS report: vaccination linked to a reduction of over a quarter million COVID-19 cases, 100,000 hospitalizations, and 39,000 deaths among seniors" ([HHS](#); see also: [ASPE report \[pdf\]](#)).

If you are in to podcasts (especially true crime or documentary format), you may want to check out WHYY's Half Vaxxed: "This is the story of a 22-year-old with no health care experience who talked his way into a COVID-19 vaccine distribution deal he thought would make him millions — only to have his company implode as thousands of people awaited vaccinations. How did he end up with so much power? And was he a grifter, or just an opportunist working the American health care system the way it's designed?" ([WHYY](#))

Boosters

With approval of Pfizer's boosters in certain groups, the FDA is considering authorizing a half-dose Moderna booster ([Bloomberg](#)).

FDA's Vaccines and Related Biological Products Advisory Committee is scheduled to meet 14 and 15 October 2021 to discuss the use of booster doses for the Moderna and Janssen/J&J vaccines ([FDA](#)).

"For people who got the J&J Vaccine, some doctors are advising boosters ASAP" ([NPR](#)).

"Covid-19 booster shots have outpaced the US rate of new vaccinations. And the millions still unvaccinated could trigger 'future waves,' expert warns" ([CNN](#)).

Vaccine Development

The Washington Post has published a series profiling 'vaccine vanguards':

- > "Serendipity and foresight prepared the world to fight the coronavirus. Barney Graham laid the groundwork for the world to battle this pandemic, and the scientists he mentored will equip us for the next one" ([WP](#)).
- > "A one-way ticket. A cash-stuffed teddy bear. A dream decades in the making. For Katalin Kariko, a life in full: Awe-inspiring ideas, careful experiments, unnoticed successes and the repeated sting of rejection" ([WP](#)).
- > "A scientific hunch. Then silence. Until the world needed a lifesaving vaccine. Drew Weissman helped make 'hugs and closeness possible again.' It didn't happen overnight" ([WP](#)).

Journal Articles

Safety, Efficacy, and Coverage

JAMA Netw Open: [Coverage and Estimated Effectiveness of mRNA COVID-19 Vaccines Among US Veterans](#) (06 October 2021)

"Question: What was the COVID-19 vaccination coverage and estimated mRNA COVID-19 vaccine effectiveness (VE) among US veterans in the first 3 months following vaccine rollout?

Findings: In this case-control study including 6 647 733 veterans, 23% of veterans received at least 1 COVID-19 vaccination during the first 3 months of vaccine rollout. VE against infection was estimated to be 95% for full vaccination; estimated VE against COVID-19-related hospitalization was 91%, and there were no COVID-19-related deaths among fully vaccinated veterans.

Meaning: These findings suggest that early vaccination rollout for veterans was efficient, and estimated VE was high for this diverse US population."

NEJM: [Waning Immune Humoral Response to BNT162b2 Covid-19 Vaccine over 6 Months](#) (06 October 2021)

"Background: Despite high vaccine coverage and effectiveness, the incidence of symptomatic infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been increasing in Israel. Whether the increasing incidence of infection is due to waning immunity after the receipt of two doses of the BNT162b2 vaccine is unclear.

Methods: We conducted a 6-month longitudinal prospective study involving vaccinated health care workers who were tested monthly for the presence of anti-spike IgG and

neutralizing antibodies. Linear mixed models were used to assess the dynamics of antibody levels and to determine predictors of antibody levels at 6 months.

Results: The study included 4868 participants, with 3808 being included in the linear mixed-model analyses. The level of IgG antibodies decreased at a consistent rate, whereas the neutralizing antibody level decreased rapidly for the first 3 months with a relatively slow decrease thereafter. Although IgG antibody levels were highly correlated with neutralizing antibody titers (Spearman's rank correlation between 0.68 and 0.75), the regression relationship between the IgG and neutralizing antibody levels depended on the time since receipt of the second vaccine dose. Six months after receipt of the second dose, neutralizing antibody titers were substantially lower among men than among women (ratio of means, 0.64; 95% confidence interval [CI], 0.55 to 0.75), lower among persons 65 years of age or older than among those 18 to less than 45 years of age (ratio of means, 0.58; 95% CI, 0.48 to 0.70), and lower among participants with immunosuppression than among those without immunosuppression (ratio of means, 0.30; 95% CI, 0.20 to 0.46).

Conclusions: Six months after receipt of the second dose of the BNT162b2 vaccine, humoral response was substantially decreased, especially among men, among persons 65 years of age or older, and among persons with immunosuppression."

NEJM: [Waning of BNT162b2 Vaccine Protection against SARS-CoV-2 Infection in Qatar](#) (06 October 2021)

"Background: Waning of vaccine protection against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection or coronavirus disease 2019 (Covid-19) is a concern. The persistence of BNT162b2 (Pfizer-BioNTech) vaccine effectiveness against infection and disease in Qatar, where the B.1.351 (or beta) and B.1.617.2 (or delta) variants have dominated incidence and polymerase-chain-reaction testing is done on a mass scale, is unclear.

Methods: We used a matched test-negative, case-control study design to estimate vaccine effectiveness against any SARS-CoV-2 infection and against any severe, critical, or fatal case of Covid-19, from January 1 to September 5, 2021.

Results: Estimated BNT162b2 effectiveness against any SARS-CoV-2 infection was negligible in the first 2 weeks after the first dose. It increased to 36.8% (95% confidence interval [CI], 33.2 to 40.2) in the third week after the first dose and reached its peak at 77.5% (95% CI, 76.4 to 78.6) in the first month after the second dose. Effectiveness declined gradually thereafter, with the decline accelerating after the fourth month to reach approximately 20% in months 5 through 7 after the second dose. Effectiveness against symptomatic infection was higher than effectiveness against asymptomatic infection but waned similarly. Variant-specific effectiveness waned in the same pattern. Effectiveness against any severe, critical, or fatal case of Covid-19 increased rapidly to 66.1% (95% CI, 56.8 to 73.5) by the third week

after the first dose and reached 96% or higher in the first 2 months after the second dose; effectiveness persisted at approximately this level for 6 months.

Conclusions: BNT162b2-induced protection against SARS-CoV-2 infection appeared to wane rapidly following its peak after the second dose, but protection against hospitalization and death persisted at a robust level for 6 months after the second dose."

Lancet: [Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study](#) (04 October 2021)

"Background: Vaccine effectiveness studies have not differentiated the effect of the delta (B.1.617.2) variant and potential waning immunity in observed reductions in effectiveness against SARS-CoV-2 infections. We aimed to evaluate overall and variant-specific effectiveness of BNT162b2 (tozinameran, Pfizer–BioNTech) against SARS-CoV-2 infections and COVID-19-related hospital admissions by time since vaccination among members of a large US health-care system.

Methods: In this retrospective cohort study, we analysed electronic health records of individuals (≥ 12 years) who were members of the health-care organisation Kaiser Permanente Southern California (CA, USA), to assess BNT162b2 vaccine effectiveness against SARS-CoV-2 infections and COVID-19-related hospital admissions for up to 6 months. Participants were required to have 1 year or more previous membership of the organisation. Outcomes comprised SARS-CoV-2 PCR-positive tests and COVID-19-related hospital admissions. Effectiveness calculations were based on hazard ratios from adjusted Cox models. This study was registered with ClinicalTrials.gov, NCT04848584.

Findings: Between Dec 14, 2020, and Aug 8, 2021, of 4 920 549 individuals assessed for eligibility, we included 3 436 957 (median age 45 years [IQR 29–61]; 1 799 395 [52·4%] female and 1 637 394 [47·6%] male). For fully vaccinated individuals, effectiveness against SARS-CoV-2 infections was 73% (95% CI 72–74) and against COVID-19-related hospital admissions was 90% (89–92). Effectiveness against infections declined from 88% (95% CI 86–89) during the first month after full vaccination to 47% (43–51) after 5 months. Among sequenced infections, vaccine effectiveness against infections of the delta variant was high during the first month after full vaccination (93% [95% CI 85–97]) but declined to 53% [39–65] after 4 months. Effectiveness against other (non-delta) variants the first month after full vaccination was also high at 97% (95% CI 95–99), but waned to 67% (45–80) at 4–5 months. Vaccine effectiveness against hospital admissions for infections with the delta variant for all ages was high overall (93% [95% CI 84–96]) up to 6 months.

Interpretation: Our results provide support for high effectiveness of BNT162b2 against hospital admissions up until around 6 months after being fully vaccinated, even in the face of widespread dissemination of the delta variant. Reduction in vaccine effectiveness against

SARS-CoV-2 infections over time is probably primarily due to waning immunity with time rather than the delta variant escaping vaccine protection."

JAMA Oncol: [Humoral Immune Response in Hematooncological Patients and Health Care Workers Who Received SARS-CoV-2 Vaccinations](#) (30 September 2021)

"Question: Do patients with cancer develop antibodies after SARS-CoV-2 vaccination, and how do their antibody levels compare with those of health care workers?

Findings: In this cohort study of 901 samples from 595 patients with hematooncological diseases and a control group of health care workers, anti-SARS-CoV-2 spike antibodies after full immunization could be detected, although antibody levels were lower in patients than in health care workers. However, specific subgroups, such as patients who received B-cell-targeting therapy, showed impaired seroconversion.

Meaning: The study findings suggest that lower SARS-CoV-2 antibody levels in patients with cancer after vaccination compared with vaccinated health care workers, and particularly weak seroconversion in specific subgroups, highlight the need for dedicated vaccination trials in patients with cancer."

NEJM: [Phase 3 Safety and Efficacy of AZD1222 \(ChAdOx1 nCoV-19\) Covid-19 Vaccine](#) (29 September 2021)

"Background: The safety and efficacy of the AZD1222 (ChAdOx1 nCoV-19) vaccine in a large, diverse population at increased risk for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in the United States, Chile, and Peru has not been known.

Methods: In this ongoing, double-blind, randomized, placebo-controlled, phase 3 clinical trial, we investigated the safety, vaccine efficacy, and immunogenicity of two doses of AZD1222 as compared with placebo in preventing the onset of symptomatic and severe coronavirus disease 2019 (Covid-19) 15 days or more after the second dose in adults, including older adults, in the United States, Chile, and Peru.

Results: A total of 32,451 participants underwent randomization, in a 2:1 ratio, to receive AZD1222 (21,635 participants) or placebo (10,816 participants). AZD1222 was safe, with low incidences of serious and medically attended adverse events and adverse events of special interest; the incidences were similar to those observed in the placebo group. Solicited local and systemic reactions were generally mild or moderate in both groups. Overall estimated vaccine efficacy was 74.0% (95% confidence interval [CI], 65.3 to 80.5; $P < 0.001$) and estimated vaccine efficacy was 83.5% (95% CI, 54.2 to 94.1) in participants 65 years of age or older. High vaccine efficacy was consistent across a range of demographic subgroups. In the fully vaccinated analysis subgroup, no severe or critical symptomatic Covid-19 cases were observed among the 17,662 participants in the AZD1222 group; 8 cases were noted among the 8550 participants in the placebo group ($< 0.1\%$). The estimated vaccine efficacy

for preventing SARS-CoV-2 infection (nucleocapsid antibody seroconversion) was 64.3% (95% CI, 56.1 to 71.0; $P < 0.001$). SARS-CoV-2 spike protein binding and neutralizing antibodies increased after the first dose and increased further when measured 28 days after the second dose.

Conclusions: AZD1222 was safe and efficacious in preventing symptomatic and severe Covid-19 across diverse populations that included older adults."

MMWR: [Safety Monitoring of an Additional Dose of COVID-19 Vaccine — United States, August 12–September 19, 2021](#) (01 October 2021, early release 28 September 2021)

"What is already known about this topic? Among 306 Pfizer-BioNTech clinical trial participants, adverse reactions after dose 3 were similar to those after dose 2.

What is added by this report? During August 12–September 19, 2021, among 12,591 v-safe registrants who completed a health check-in survey after all 3 doses of an mRNA COVID-19 vaccine, 79.4% and 74.1% reported local or systemic reactions, respectively, after the third dose; 77.6% and 76.5% reported local or systemic reactions after the second dose, respectively.

What are the implications for public health practice? Voluntary reports to v-safe found no unexpected patterns of adverse reactions after an additional dose of COVID-19 vaccine. CDC will continue to monitor vaccine safety, including for additional COVID-19 doses."

Adverse Events/Side Effects

JAMA: [Association of Receipt of the Ad26.COV2.S COVID-19 Vaccine With Presumptive Guillain-Barré Syndrome, February-July 2021](#) (07 October 2021)

"Question: In a passive reporting system, is there an association between receipt of the Ad26.COV2.S (Janssen/Johnson & Johnson) COVID-19 vaccine and development of Guillain-Barré syndrome (GBS)?

Findings: Within the US Vaccine Adverse Event Reporting System (VAERS), 130 cases of presumptive GBS were reported from February 2021 to July 2021. The overall estimated observed to expected rate ratio was 4.18, corresponding to an absolute rate increase of 6.36 per 100 000 person-years.

Meaning: These findings suggest a potential small but statistically significant safety concern for Guillain-Barré syndrome following receipt of the Ad26.COV2.S vaccine but are considered preliminary pending analysis of medical records to establish a definitive diagnosis."

NEJM: [Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel](#) (06 October 2021)

"Background: Approximately 5.1 million Israelis had been fully immunized against coronavirus disease 2019 (Covid-19) after receiving two doses of the BNT162b2 messenger RNA vaccine (Pfizer-BioNTech) by May 31, 2021. After early reports of myocarditis during adverse events monitoring, the Israeli Ministry of Health initiated active surveillance.

Methods: We retrospectively reviewed data obtained from December 20, 2020, to May 31, 2021, regarding all cases of myocarditis and categorized the information using the Brighton Collaboration definition. We analyzed the occurrence of myocarditis by computing the risk difference for the comparison of the incidence after the first and second vaccine doses (21 days apart); by calculating the standardized incidence ratio of the observed-to-expected incidence within 21 days after the first dose and 30 days after the second dose, independent of certainty of diagnosis; and by calculating the rate ratio 30 days after the second dose as compared with unvaccinated persons.

Results: Among 304 persons with symptoms of myocarditis, 21 had received an alternative diagnosis. Of the remaining 283 cases, 142 occurred after receipt of the BNT162b2 vaccine; of these cases, 136 diagnoses were definitive or probable. The clinical presentation was judged to be mild in 129 recipients (95%); one fulminant case was fatal. The overall risk difference between the first and second doses was 1.76 per 100,000 persons (95% confidence interval [CI], 1.33 to 2.19), with the largest difference among male recipients between the ages of 16 and 19 years (difference, 13.73 per 100,000 persons; 95% CI, 8.11 to 19.46). As compared with the expected incidence based on historical data, the standardized incidence ratio was 5.34 (95% CI, 4.48 to 6.40) and was highest after the second dose in male recipients between the ages of 16 and 19 years (13.60; 95% CI, 9.30 to 19.20). The rate ratio 30 days after the second vaccine dose in fully vaccinated recipients, as compared with unvaccinated persons, was 2.35 (95% CI, 1.10 to 5.02); the rate ratio was again highest in male recipients between the ages of 16 and 19 years (8.96; 95% CI, 4.50 to 17.83), with a ratio of 1 in 6637.

Conclusions: The incidence of myocarditis, although low, increased after the receipt of the BNT162b2 vaccine, particularly after the second dose among young male recipients. The clinical presentation of myocarditis after vaccination was usually mild."

NEJM: [Myocarditis after Covid-19 Vaccination in a Large Health Care Organization](#) (06 October 2021)

"Background: Reports have suggested an association between the development of myocarditis and the receipt of messenger RNA (mRNA) vaccines against coronavirus disease 2019 (Covid-19), but the frequency and severity of myocarditis after vaccination have not been extensively explored.

Methods: We searched the database of Clalit Health Services, the largest health care organization (HCO) in Israel, for diagnoses of myocarditis in patients who had received at least one dose of the BNT162b2 mRNA vaccine (Pfizer-BioNTech). The diagnosis of myocarditis was adjudicated by cardiologists using the case definition used by the Centers for Disease Control and Prevention. We abstracted the presentation, clinical course, and outcome from the patient's electronic health record. We performed a Kaplan-Meier analysis of the incidence of myocarditis up to 42 days after the first vaccine dose.

Results: Among more than 2.5 million vaccinated HCO members who were 16 years of age or older, 54 cases met the criteria for myocarditis. The estimated incidence per 100,000 persons who had received at least one dose of vaccine was 2.13 cases (95% confidence interval [CI], 1.56 to 2.70). The highest incidence of myocarditis (10.69 cases per 100,000 persons; 95% CI, 6.93 to 14.46) was reported in male patients between the ages of 16 and 29 years. A total of 76% of cases of myocarditis were described as mild and 22% as intermediate; 1 case was associated with cardiogenic shock. After a median follow-up of 83 days after the onset of myocarditis, 1 patient had been readmitted to the hospital, and 1 had died of an unknown cause after discharge. Of 14 patients who had left ventricular dysfunction on echocardiography during admission, 10 still had such dysfunction at the time of hospital discharge. Of these patients, 5 underwent subsequent testing that revealed normal heart function.

Conclusions: Among patients in a large Israeli health care system who had received at least one dose of the BNT162b2 mRNA vaccine, the estimated incidence of myocarditis was 2.13 cases per 100,000 persons; the highest incidence was among male patients between the ages of 16 and 29 years. Most cases of myocarditis were mild or moderate in severity."

JAMA Intern Med: [Acute Myocarditis Following COVID-19 mRNA Vaccination in Adults Aged 18 Years or Older](#) (04 October 2021)

"This cohort study examines the incidence and clinical outcomes of acute myocarditis among adults following mRNA vaccination in an integrated health care system in the US....

In this population-based cohort study of 2 392 924 individuals who received at least 1 dose of COVID-19 mRNA vaccines, acute myocarditis was rare, at an incidence of 5.8 cases per 1 million individuals after the second dose (1 case per 172 414 fully vaccinated individuals). The signal of increased myocarditis in young men warrants further investigation."

JAMA Neurol: [Characteristics and Outcomes of Patients With Cerebral Venous Sinus Thrombosis in SARS-CoV-2 Vaccine–Induced Immune Thrombotic Thrombocytopenia](#) (28 September 2021)

"Question: What are the clinical characteristics and outcomes of patients with cerebral venous sinus thrombosis with thrombocytopenia syndrome after SARS-CoV-2 vaccination?"

Findings: In this cohort study of 116 patients with cerebral venous sinus thrombosis after SARS-CoV-2 vaccination, 78 (67.2%) had thrombosis with thrombocytopenia syndrome. Patients with thrombosis with thrombocytopenia syndrome were frequently comatose at presentation (24%) and often had intracerebral hemorrhage (68%) and concomitant thromboembolism (36%), and 47% died during hospitalization.

Meaning: Patients with cerebral venous sinus thrombosis after SARS-CoV-2 vaccination who met criteria for thrombosis with thrombocytopenia syndrome had a distinct clinical profile and high mortality rate."

Vaccine Hesitancy and Decision Making

JAMA Netw Open: [COVID-19 Vaccine Decision-making Factors in Racial and Ethnic Minority Communities in Los Angeles, California](#) (30 September 2021)

"Question: What factors do members of multiethnic communities at high risk for COVID-19 infection and morbidity in Los Angeles County, California, cite as influencing vaccine decision-making and acceptability?

Findings: In this qualitative study, 70 participants from racial and ethnic minority communities in Los Angeles County described a complex vaccination decision-making process influenced by misinformation and politicization, deep apprehension related to historical inequity and mistreatment, access barriers related to social disadvantage, and a need for community engagement and trusted messengers.

Meaning: This study suggests that COVID-19 vaccine equity will require multifaceted policies and programming that respect community concerns and the need for informed deliberation, invest in community-based engagement, improve accessibility and transparency of information, and reduce structural barriers in vaccination."

JAMA Netw Open: [Trajectory of COVID-19 Vaccine Hesitancy Over Time and Association of Initial Vaccine Hesitancy With Subsequent Vaccination](#) (24 September 2021)

"This cohort study found that COVID-19 vaccine hesitancy is not a stable trait precluding vaccination but, instead, is labile. Hesitancy decreased between late 2020 and early 2021, with nearly one-third (32%) of persons who were initially hesitant being vaccinated at follow-up and more than one-third (37%) transitioning from vaccine hesitant into vaccine willing. Early plans regarding vaccination frequently deviated from later action in vaccine seeking. Self-reported vaccination status was congruent with biological tests, indicating that it is a valid metric. Changes in hesitancy have not alleviated health inequities in vaccines received, and further studies are needed to explore the reasons why vaccine hesitancy is changing over time by group."

Breakthrough Infections, Reinfections, and Coinfections

News in Brief

"I got a 'mild' breakthrough case. Here's what i wish I'd known" ([KHN](#)).

"Woman who survived 1918 flu, world war succumbs to COVID" ([AP](#)).

Journal Articles

World Psychiatry: [Increased risk for COVID-19 breakthrough infection in fully vaccinated patients with substance use disorders in the United States between December 2020 and August 2021](#) (05 October 2021)

"Individuals with substance use disorders (SUDs) are at increased risk for COVID-19 infection and for adverse outcomes of the infection. Though vaccines are highly effective against COVID-19, their effectiveness in individuals with SUDs might be curtailed by compromised immune status and a greater likelihood of exposures, added to the waning vaccine immunity and the new SARS-CoV-2 variants.

In a population-based cohort study, we assessed the risk, time trends, outcomes and disparities of COVID-19 breakthrough infection in fully vaccinated SUD patients starting 14 days after completion of vaccination. The study included 579,372 individuals (30,183 with a diagnosis of SUD and 549,189 without such a diagnosis) who were fully vaccinated between December 2020 and August 2021, and had not contracted COVID-19 infection prior to vaccination. We used the TriNetX Analytics network platform to access de-identified electronic health records from 63 health care organizations in the US.

Among SUD patients, the risk for breakthrough infection ranged from 6.8% for tobacco use disorder to 7.8% for cannabis use disorder, all significantly higher than the 3.6% in non-SUD population ($p < 0.001$). Breakthrough infection risk remained significantly higher after controlling for demographics (age, gender, ethnicity) and vaccine types for all SUD subtypes, except for tobacco use disorder, and was highest for cocaine and cannabis use disorders (hazard ratio, HR=2.06, 95% CI: 1.30-3.25 for cocaine; HR=1.92, 95% CI: 1.39-2.66 for cannabis). When we matched SUD and non-SUD individuals for lifetime comorbidities and adverse socioeconomic determinants of health, the risk for breakthrough infection no longer differed between these populations, except for patients with cannabis use disorder, who remained at increased risk (HR=1.55, 95% CI: 1.22-1.99). The risk for breakthrough infection was higher in SUD patients who received the Pfizer than the Moderna vaccine (HR=1.49, 95% CI: 1.31-1.69). In the vaccinated SUD population, the risk for hospitalization was 22.5% for the breakthrough cohort and 1.6% for the non-breakthrough cohort (risk ratio, RR=14.4, 95% CI: 10.19-20.42), while the risk for death was 1.7% and 0.5%

respectively (RR=3.5, 95% CI: 1.74-7.05). No significant age, gender and ethnic disparities for breakthrough infection were observed in vaccinated SUD patients.

These data suggest that fully vaccinated SUD individuals are at higher risk for breakthrough COVID-19 infection, and this is largely due to their higher prevalence of comorbidities and adverse socioeconomic determinants of health compared with non-SUD individuals. The high frequency of comorbidities in SUD patients is also likely to contribute to their high rates of hospitalization and death following breakthrough infection."

Lancet Microbe: [The durability of immunity against reinfection by SARS-CoV-2: a comparative evolutionary study](#) (01 October 2021)

"Background: Among the most consequential unknowns of the devastating COVID-19 pandemic are the durability of immunity and time to likely reinfection. There are limited direct data on SARS-CoV-2 long-term immune responses and reinfection. The aim of this study is to use data on the durability of immunity among evolutionarily close coronavirus relatives of SARS-CoV-2 to estimate times to reinfection by a comparative evolutionary analysis of related viruses SARS-CoV, MERS-CoV, human coronavirus (HCoV)-229E, HCoV-OC43, and HCoV-NL63.

Methods: We conducted phylogenetic analyses of the S, M, and ORF1b genes to reconstruct a maximum-likelihood molecular phylogeny of human-infecting coronaviruses. This phylogeny enabled comparative analyses of peak-normalised nucleocapsid protein, spike protein, and whole-virus lysate IgG antibody optical density levels, in conjunction with reinfection data on endemic human-infecting coronaviruses. We performed ancestral and descendent states analyses to estimate the expected declines in antibody levels over time, the probabilities of reinfection based on antibody level, and the anticipated times to reinfection after recovery under conditions of endemic transmission for SARS-CoV-2, as well as the other human-infecting coronaviruses.

Findings: We obtained antibody optical density data for six human-infecting coronaviruses, extending from 128 days to 28 years after infection between 1984 and 2020. These data provided a means to estimate profiles of the typical antibody decline and probabilities of reinfection over time under endemic conditions. Reinfection by SARS-CoV-2 under endemic conditions would likely occur between 3 months and 5.1 years after peak antibody response, with a median of 16 months. This protection is less than half the duration revealed for the endemic coronaviruses circulating among humans (5–95% quantiles 15 months to 10 years for HCoV-OC43, 31 months to 12 years for HCoV-NL63, and 16 months to 12 years for HCoV-229E). For SARS-CoV, the 5–95% quantiles were 4 months to 6 years, whereas the 95% quantiles for MERS-CoV were inconsistent by dataset.

Interpretation: The timeframe for reinfection is fundamental to numerous aspects of public health decision making. As the COVID-19 pandemic continues, reinfection is likely to

become increasingly common. Maintaining public health measures that curb transmission—including among individuals who were previously infected with SARS-CoV-2—coupled with persistent efforts to accelerate vaccination worldwide is critical to the prevention of COVID-19 morbidity and mortality."

Treatments and Management

News in Brief

AstraZeneca has applied for a EUA for its antibody cocktail used as COVID-19 prophylaxis ([AstraZeneca](#)).

"A daily pill to treat Covid could be just months away, scientists say" ([KHN](#)).

"What we know — and don't know — about Merck's new Covid-19 pill" ([STAT](#); see also: [other STAT article](#) and [Merck's news release about molnupiravir](#)).

"AstraZeneca has requested emergency approval from U.S. regulators for its antibody cocktail, the first protective shot other than vaccines against COVID-19" ([Reuters](#)).

"On new recommendation for treatment of COVID-19 patients: WHO calls for equitable access to casirivimab and imdevimab for COVID-19" ([WHO](#)).

Journal Articles

JAMA Intern Med: [Efficacy and Safety of Therapeutic-Dose Heparin vs Standard Prophylactic or Intermediate-Dose Heparins for Thromboprophylaxis in High-risk Hospitalized Patients With COVID-19: The HEP-COVID Randomized Clinical Trial](#) (07 October 2021)

"Question: Does thromboprophylaxis with therapeutic-dose low-molecular-weight heparin reduce the incidence of major thromboembolism and death compared with prophylactic/intermediate-dose heparins in inpatients with high-risk COVID-19?

Findings: In this randomized clinical trial of 253 adults, the incidence of major thromboembolism or death was 28.7% with therapeutic-dose vs 41.9% with prophylactic/intermediate-dose heparins, a significant difference—driven by reduction in thromboembolism—that was not seen in critically ill patients. There was no significant difference in major bleeding between groups.

Meaning: Thromboprophylaxis with therapeutic-dose low-molecular-weight heparin reduces a composite outcome of major thromboembolism and death in high-risk inpatients with COVID-19."

JAMA: [Effect of Convalescent Plasma on Organ Support-Free Days in Critically Ill Patients With COVID-19: A Randomized Clinical Trial](#) (04 October 2021)

"Question: Does 2 units of ABO-compatible, high-titer convalescent plasma, administered to critically ill patients with COVID-19, improve organ support-free days up to day 21 (a composite end point of in-hospital mortality and the duration of intensive care unit-based respiratory or cardiovascular support)?

Findings: This international bayesian randomized clinical trial that included 2011 participants treated with 2 units of high-titer convalescent plasma, compared with no convalescent plasma, resulted in a posterior probability of futility of 99.4% for the primary outcome of organ support-free days up to day 21.

Meaning: Among critically ill adults with confirmed COVID-19, treatment with convalescent plasma had a low likelihood of providing improvement in organ support-free days."

Clin Infect Dis: [Remdesivir treatment in hospitalized patients with COVID-19: a comparative analysis of in-hospital all-cause mortality in a large multi-center observational cohort](#) (01 October 2021)

"Background: Remdesivir (RDV) improved clinical outcomes among hospitalized COVID-19 patients in randomized trials, but data from clinical practice are limited.

Methods: We examined survival outcomes for US patients hospitalized with COVID-19 between Aug-Nov 2020 and treated with RDV within two-days of hospitalization vs. those not receiving RDV during their hospitalization using the Premier Healthcare Database. Preferential within-hospital propensity score matching with replacement was used. Additionally, patients were also matched on baseline oxygenation level (no supplemental oxygen charges (NSO), low-flow oxygen (LFO), high-flow oxygen/non-invasive ventilation (HFO/NIV) and invasive mechanical ventilation/ECMO (IMV/ECMO) and two-month admission window and excluded if discharged within 3-days of admission (to exclude anticipated discharges/transfers within 72-hrs consistent with ACTT-1 study). Cox Proportional Hazards models were used to assess time to 14-/28-day mortality overall and for patients on NSO, LFO, HFO/NIV and IMV/ECMO.

Results: 28,855 RDV patients were matched to 16,687 unique non-RDV patients. Overall, 10.6% and 15.4% RDV patients died within 14- and 28-days, respectively compared with 15.4% and 19.1% non-RDV patients. Overall, RDV was associated with a reduction in mortality at 14-days (HR[95% CI]: 0.76[0.70-0.83]) and 28-days (0.89[0.82-0.96]). This mortality benefit was also seen for NSO, LFO and IMV/ECMO at 14-days (NSO:0.69[0.57-

0.83], LFO:0.68[0.80-0.77], IMV/ECMO:0.70[0.58-0.84]) and 28-days (NSO:0.80[0.68-0.94], LFO:0.77[0.68-0.86], IMV/ECMO:0.81[0.69-0.94]). Additionally, HFO/NIV RDV group had a lower risk of mortality at 14-days (0.81[0.70-0.93]) but no statistical significance at 28-days.

Conclusions: RDV initiated upon hospital admission was associated with improved survival among COVID-19 patients. Our findings complement ACTT-1 and support RDV as a foundational treatment for hospitalized COVID-19 patients."

Lancet: [Extracorporeal membrane oxygenation for COVID-19: evolving outcomes from the international Extracorporeal Life Support Organization Registry](#) (29 September 2021)

"Background: Over the course of the COVID-19 pandemic, the care of patients with COVID-19 has changed and the use of extracorporeal membrane oxygenation (ECMO) has increased. We aimed to examine patient selection, treatments, outcomes, and ECMO centre characteristics over the course of the pandemic to date.

Methods: We retrospectively analysed the Extracorporeal Life Support Organization Registry and COVID-19 Addendum to compare three groups of ECMO-supported patients with COVID-19 (aged ≥ 16 years). At early-adopting centres-ie, those using ECMO support for COVID-19 throughout 2020-we compared patients who started ECMO on or before May 1, 2020 (group A1), and between May 2 and Dec 31, 2020 (group A2). Late-adopting centres were those that provided ECMO for COVID-19 only after May 1, 2020 (group B). The primary outcome was in-hospital mortality in a time-to-event analysis assessed 90 days after ECMO initiation. A Cox proportional hazards model was fit to compare the patient and centre-level adjusted relative risk of mortality among the groups.

Findings: In 2020, 4812 patients with COVID-19 received ECMO across 349 centres within 41 countries. For early-adopting centres, the cumulative incidence of in-hospital mortality 90 days after ECMO initiation was 36.9% (95% CI 34.1-39.7) in patients who started ECMO on or before May 1 (group A1) versus 51.9% (50.0-53.8) after May 1 (group A2); at late-adopting centres (group B), it was 58.9% (55.4-62.3). Relative to patients in group A2, group A1 patients had a lower adjusted relative risk of in-hospital mortality 90 days after ECMO (hazard ratio 0.82 [0.70-0.96]), whereas group B patients had a higher adjusted relative risk (1.42 [1.17-1.73]).

Interpretation: Mortality after ECMO for patients with COVID-19 worsened during 2020. These findings inform the role of ECMO in COVID-19 for patients, clinicians, and policy makers."

NEJM: [REGEN-COV Antibody Combination and Outcomes in Outpatients with Covid-19](#) (28 September 2021)

"Background: In the phase 1-2 portion of an adaptive trial, REGEN-COV, a combination of the monoclonal antibodies casirivimab and imdevimab, reduced the viral load and number

of medical visits in patients with coronavirus disease 2019 (Covid-19). REGEN-COV has activity in vitro against current severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants of concern.

Methods: In the phase 3 portion of an adaptive trial, we randomly assigned outpatients with Covid-19 and risk factors for severe disease to receive various doses of intravenous REGEN-COV or placebo. Patients were followed through day 29. A prespecified hierarchical analysis was used to assess the end points of hospitalization or death and the time to resolution of symptoms. Safety was also evaluated.

Results: Covid-19-related hospitalization or death from any cause occurred in 18 of 1355 patients in the REGEN-COV 2400-mg group (1.3%) and in 62 of 1341 patients in the placebo group who underwent randomization concurrently (4.6%) (relative risk reduction [1 minus the relative risk], 71.3%; $P < 0.001$); these outcomes occurred in 7 of 736 patients in the REGEN-COV 1200-mg group (1.0%) and in 24 of 748 patients in the placebo group who underwent randomization concurrently (3.2%) (relative risk reduction, 70.4%; $P = 0.002$). The median time to resolution of symptoms was 4 days shorter with each REGEN-COV dose than with placebo (10 days vs. 14 days; $P < 0.001$ for both comparisons). REGEN-COV was efficacious across various subgroups, including patients who were SARS-CoV-2 serum antibody-positive at baseline. Both REGEN-COV doses reduced viral load faster than placebo; the least-squares mean difference in viral load from baseline through day 7 was $-0.71 \log_{10}$ copies per milliliter (95% confidence interval [CI], -0.90 to -0.53) in the 1200-mg group and $-0.86 \log_{10}$ copies per milliliter (95% CI, -1.00 to -0.72) in the 2400-mg group. Serious adverse events occurred more frequently in the placebo group (4.0%) than in the 1200-mg group (1.1%) and the 2400-mg group (1.3%); infusion-related reactions of grade 2 or higher occurred in less than 0.3% of the patients in all groups.

Conclusions: REGEN-COV reduced the risk of Covid-19-related hospitalization or death from any cause, and it resolved symptoms and reduced the SARS-CoV-2 viral load more rapidly than placebo."

EClinicalMedicine: [Outpatient and inpatient anticoagulation therapy and the risk for hospital admission and death among COVID-19 patients](#) (24 September 2021)

"Background: Coronavirus disease 2019 (COVID-19) is associated with a hypercoagulable state. Limited data exist informing the relationship between anticoagulation therapy and risk for COVID-19 related hospitalization and mortality.

Methods: We evaluated all patients over the age of 18 diagnosed with COVID-19 in a prospective cohort study from March 4th to August 27th, 2020 among 12 hospitals and 60 clinics of M Health Fairview system (USA). We investigated the relationship between (1) 90-day anticoagulation therapy among outpatients before COVID-19 diagnosis and the risk for hospitalization and mortality and (2) Inpatient anticoagulation therapy and mortality risk.

Findings: Of 6195 patients, 598 were immediately hospitalized and 5597 were treated as outpatients. The overall case-fatality rate was 2.8% (n = 175 deaths). Among the patients who were hospitalized, the inpatient mortality was 13%. Among the 5597 COVID-19 patients initially treated as outpatients, 160 (2.9%) were on anticoagulation and 331 were eventually hospitalized (5.9%). In a multivariable analysis, outpatient anticoagulation use was associated with a 43% reduction in risk for hospital admission, HR (95% CI = 0.57, 0.38–0.86), p = 0.007, but was not associated with mortality, HR (95% CI=0.88, 0.50 - 1.52), p = 0.64. Inpatients who were not on anticoagulation (before or after hospitalization) had an increased risk for mortality, HR (95% CI = 2.26, 1.17–4.37), p = 0.015.

Interpretation: Outpatients with COVID-19 who were on outpatient anticoagulation at the time of diagnosis experienced a 43% reduced risk of hospitalization. Failure to initiate anticoagulation upon hospitalization or maintaining outpatient anticoagulation in hospitalized COVID-19 patients was associated with increased mortality risk."

Pre-Existing Conditions, Comorbidities, and Impact on Other Health Issues

Journal Articles

Lancet Oncol: [Effect of COVID-19 pandemic lockdowns on planned cancer surgery for 15 tumour types in 61 countries: an international, prospective, cohort study](#) (05 October 2021)

"Background: Surgery is the main modality of cure for solid cancers and was prioritised to continue during COVID-19 outbreaks. This study aimed to identify immediate areas for system strengthening by comparing the delivery of elective cancer surgery during the COVID-19 pandemic in periods of lockdown versus light restriction.

Methods: This international, prospective, cohort study enrolled 20 006 adult (≥18 years) patients from 466 hospitals in 61 countries with 15 cancer types, who had a decision for curative surgery during the COVID-19 pandemic and were followed up until the point of surgery or cessation of follow-up (Aug 31, 2020). Average national Oxford COVID-19 Stringency Index scores were calculated to define the government response to COVID-19 for each patient for the period they awaited surgery, and classified into light restrictions (index <20), moderate lockdowns (20–60), and full lockdowns (>60). The primary outcome was the non-operation rate (defined as the proportion of patients who did not undergo planned surgery). Cox proportional-hazards regression models were used to explore the associations between lockdowns and non-operation. Intervals from diagnosis to surgery were compared across COVID-19 government response index groups. This study was registered at ClinicalTrials.gov, NCT04384926.

Findings: Of eligible patients awaiting surgery, 2003 (10.0%) of 20 006 did not receive surgery after a median follow-up of 23 weeks (IQR 16–30), all of whom had a COVID-19-related reason given for non-operation. Light restrictions were associated with a 0.6% non-operation rate (26 of 4521), moderate lockdowns with a 5.5% rate (201 of 3646; adjusted hazard ratio [HR] 0.81, 95% CI 0.77–0.84; $p < 0.0001$), and full lockdowns with a 15.0% rate (1775 of 11 827; HR 0.51, 0.50–0.53; $p < 0.0001$). In sensitivity analyses, including adjustment for SARS-CoV-2 case notification rates, moderate lockdowns (HR 0.84, 95% CI 0.80–0.88; $p < 0.001$), and full lockdowns (0.57, 0.54–0.60; $p < 0.001$), remained independently associated with non-operation. Surgery beyond 12 weeks from diagnosis in patients without neoadjuvant therapy increased during lockdowns (374 [9.1%] of 4521 in light restrictions, 317 [10.4%] of 3646 in moderate lockdowns, 2001 [23.8%] of 11 827 in full lockdowns), although there were no differences in resectability rates observed with longer delays.

Interpretation: Cancer surgery systems worldwide were fragile to lockdowns, with one in seven patients who were in regions with full lockdowns not undergoing planned surgery and experiencing longer preoperative delays. Although short-term oncological outcomes were not compromised in those selected for surgery, delays and non-operations might lead to long-term reductions in survival. During current and future periods of societal restriction, the resilience of elective surgery systems requires strengthening, which might include protected elective surgical pathways and long-term investment in surge capacity for acute care during public health emergencies to protect elective staff and services."

PLoS One: [Severe COVID-19 in inflammatory bowel disease patients in a population-based setting](#) (05 October 2021)

"Objective: Data on the course of severe COVID-19 in inflammatory bowel disease (IBD) patients remains limited. We aimed to determine the incidence rate and clinical course of severe COVID-19 in the heavily affected South-Limburg region in the Netherlands.

Methods: All COVID-19 patients admitted to the only two hospitals covering the whole South-Limburg region between February 27, 2020 and January 4, 2021 were included. Incidence rates for hospitalization due to COVID-19 were determined for the IBD ($n = 4980$) and general population ($n = 597,184$) in South-Limburg.

Results: During a follow-up of 4254 and 510,120 person-years, 20 IBD patients (0.40%; 11 ulcerative colitis (UC), 9 Crohn's disease (CD)) and 1425 (0.24%) patients from the general population were hospitalized due to proven COVID-19 corresponding to an incidence rate of 4.7 (95% Confidence interval (CI) 3.0–7.1) and 2.8 (95% CI 2.6–2.9) per 1000 patient years, respectively (Incidence rate ratio: 1.68, 95% CI 1.08–2.62, $p = 0.019$). Median age (IBD: 63.0 (IQR 58.0–75.8) years vs. general population: 72.0 (IQR 62.0–80.0) years, $p = 0.10$) and mean BMI (IBD: 24.4 (SD 3.3) kg/m² vs. general population 24.1 (SD 4.9) kg/m², $p = 0.79$) at admission were comparable in both populations. As for course of severe COVID-19, similar

rates of ICU admission (IBD: 12.5% vs. general population: 15.7%, $p = 1.00$), mechanical ventilation (6.3% vs. 11.2%, $p = 1.00$) and death were observed (6.3% vs. 21.8%, $p = 0.22$).

Conclusion: We found a statistically significant higher rate of hospitalization due to COVID-19 in IBD patients in a population-based setting in a heavily impacted Dutch region. This finding reflects previous research that showed IBD patients using systemic medication were at an increased risk of serious infection. However, although at an increased risk of hospitalization, clinical course of severe COVID-19 was comparable to hospitalized patients without IBD."

Clin Infect Dis: [Changing patterns of bloodstream infections in the community and acute care across two COVID-19 epidemic waves: a retrospective analysis using data linkage](#) (01 October 2021)

"Background: We examined the epidemiology of community- and hospital-acquired bloodstream infections (BSIs) in COVID-19 and non-COVID-19 patients across two epidemic waves.

Methods: We analysed blood cultures of patients presenting and admitted to a London hospital group between January 2020 and February 2021. We reported BSI incidence, as well as changes in sampling, case mix, healthcare capacity, and COVID-19 variants.

Results: 34,044 blood cultures were taken. We identified 1,047 BSIs; 653 (62.4%) community-acquired and 394 (37.6%) hospital-acquired. Important changes in patterns were seen. Among community-acquired BSIs, *Escherichia coli* BSIs remained lower than pre-pandemic level during COVID-19 waves, however peaked following lockdown easing in May 2020, deviating from the historical trend of peaking in August. The hospital-acquired BSI rate was 100.4 per 100,000 patient-days across the pandemic, increasing to 132.3 during the first wave and 190.9 during the second, with significant increase seen in elective inpatients. Patients who developed a hospital-acquired BSI, including those without COVID-19, experienced 20.2 excess days of hospital stay and 26.7% higher mortality, higher than reported in pre-pandemic literature. In intensive care, the BSI rate was 421.0 per 100,000 patient-ICU days during the second wave, compared to 101.3 pre-COVID. The BSI incidence in those infected with the SARS-CoV-2 Alpha variant was similar to that seen with earlier variants.

Conclusions: The pandemic and national responses have impacted the patterns of community- and hospital-acquired BSIs, in COVID-19 and non-COVID-19 patients. Factors driving the observed patterns are complex. Infection surveillance needs to consider key aspects of pandemic response and changes in healthcare access and practice."

Emerg Infect Dis: [Outbreak of Mucormycosis in Coronavirus Disease Patients, Pune, India](#) (29 September 2021)

"We provide an overview of the epidemiology and clinical course of mucormycosis in the coronavirus disease (COVID-19) pandemic era. We conducted a retrospective chart review of 178 patients with clinical or diagnostic, endoscopically or histopathologically confirmed rhino-sino-orbital or cerebral mucormycosis after COVID-19 treatment during the second wave of COVID-19 in Pune, India. Median time to symptom onset from COVID-19 detection was 28 days. Moderate or severe COVID-19 was seen in 73% of patients and diabetes in 74.2%. A total of 52.8% received steroids. Eschar over or inside the nose was seen in 75%, but baseline clinical and laboratory parameters were mostly unremarkable. Bone penetration was present in ≈90% of cases, 30% had soft-tissue swelling of the pterygopalatine fossa and 7% had cavernous sinus thrombosis, and 60% had multifocal mucormycosis. Of the 178 study cases, 151 (85%) underwent surgical debridement. Twenty-six (15%) died, and 16 (62%) of those had multifocal mucormycosis."

J Clin Endocrinol Metab: [Age and Hospitalization Risk in People With Type 1 Diabetes and COVID-19: Data From the T1D Exchange Surveillance Study](#) (28 September 2021)

"Context: COVID-19 morbidity and mortality are increased in type 1 diabetes (T1D), but few data focus on age-based outcomes.

Objective: To quantify the risk for COVID-19 related hospitalization and adverse outcomes by age in people with T1D.

Design, setting and patients: For this observational, multisite, cross-sectional study of patients with T1D and laboratory-confirmed COVID-19 from 56 clinical sites in the United States, data were collected from April 2020 to March 2021. The distribution of patient factors and outcomes across age groups (0-18, 19-40 and > 40 years) was examined. Descriptive statistics were used to describe the study population, and multivariate logistic regression models were used to analyze the relationship between age, adverse outcomes, and hospitalization.

Main outcome measures: Hospitalization for COVID-19.

Results: A total of 767 patients were analyzed. Fifty-four percent (n=415) were aged 0-18 years, thirty-two percent (n=247) were aged 19-40 years and fourteen percent (n=105) were aged >40 years. One-hundred and seventy patients were hospitalized, and 5 patients died. Compared to the 0-18 years age group, those >40 years of age had an adjusted odds ratio of 4.2 (95% confidence interval 2.28-7.83) for hospitalization after adjustment for gender, A1c, race, insurance type and comorbidities.

Conclusions: Age >40 years is a risk factor for patients with T1D and COVID-19, with children and younger adults experiencing milder disease and better prognosis. This indicates a need for age-tailored treatments, immunization, and clinical management of individuals affected by T1D."

Thorax: [Smoking and COVID-19 outcomes: an observational and Mendelian randomisation study using the UK Biobank cohort](#) (27 September 2021)

"Background: Conflicting evidence has emerged regarding the relevance of smoking on risk of COVID-19 and its severity.

Methods: We undertook large-scale observational and Mendelian randomisation (MR) analyses using UK Biobank. Most recent smoking status was determined from primary care records (70.8%) and UK Biobank questionnaire data (29.2%). COVID-19 outcomes were derived from Public Health England SARS-CoV-2 testing data, hospital admissions data, and death certificates (until 18 August 2020). Logistic regression was used to estimate associations between smoking status and confirmed SARS-CoV-2 infection, COVID-19-related hospitalisation, and COVID-19-related death. Inverse variance-weighted MR analyses using established genetic instruments for smoking initiation and smoking heaviness were undertaken (reported per SD increase).

Results: There were 421 469 eligible participants, 1649 confirmed infections, 968 COVID-19-related hospitalisations and 444 COVID-19-related deaths. Compared with never-smokers, current smokers had higher risks of hospitalisation (OR 1.80, 95% CI 1.26 to 2.29) and mortality (smoking 1-9/day: OR 2.14, 95% CI 0.87 to 5.24; 10-19/day: OR 5.91, 95% CI 3.66 to 9.54; 20+/day: OR 6.11, 95% CI 3.59 to 10.42). In MR analyses of 281 105 White British participants, genetically predicted propensity to initiate smoking was associated with higher risks of infection (OR 1.45, 95% CI 1.10 to 1.91) and hospitalisation (OR 1.60, 95% CI 1.13 to 2.27). Genetically predicted higher number of cigarettes smoked per day was associated with higher risks of all outcomes (infection OR 2.51, 95% CI 1.20 to 5.24; hospitalisation OR 5.08, 95% CI 2.04 to 12.66; and death OR 10.02, 95% CI 2.53 to 39.72).

Interpretation: Congruent results from two analytical approaches support a causal effect of smoking on risk of severe COVID-19."

Disaster Med Public Health Prep: [Treating an Epidemic During a Pandemic: Experience Treating Opioid Use Disorder at the Baltimore Convention Center Field Hospital](#) (21 September 2021)

"During the COVID-19 pandemic, access to addiction treatment has plummeted. At the same time, patients with opioid use disorder are at higher risk for COVID-19 infection and experience worse outcomes. The Baltimore Convention Center Field Hospital (BCCFH), a state-run COVID-19 disaster hospital operated by Johns Hopkins Medicine and the University of Maryland Medical System, continues to operate 14 months into the pandemic to serve as an overflow unit for the state's hospitals. BCCFH staff observed the demand for opioid use disorder care and developed admission criteria, a pharmacy formulary, and case management procedures to meet this need. This article describes generalized lessons from the BCCFH experience treating substance use disorder during a pandemic."

Long COVID / Post-COVID Period

News in Brief

"Long Covid now has an official definition from the World Health Organization — Lingering fatigue, shortness of breath, and brain fog are among the symptoms people may experience months after infection, the WHO says" ([Gizmodo](#); see also: [WHO report](#)).

Journal Articles

Sci Immunol: [Immune signatures underlying post-acute COVID-19 lung sequelae](#) (30 September 2021)

"Severe COVID-19 pneumonia survivors often exhibit long-term pulmonary sequelae, but the underlying mechanisms or associated local and systemic immune correlates are not known. Here, we have performed high-dimensional characterization of the pathophysiological and immune traits of aged COVID-19 convalescents, and correlated the local and systemic immune profiles with pulmonary function and lung imaging. We found that chronic lung impairment was accompanied by persistent respiratory immune alterations. We showed that functional SARS-CoV-2-specific memory T and B cells were enriched at the site of infection compared to those of blood. Detailed evaluation of the lung immune compartment revealed dysregulated respiratory CD8+ T cell responses were associated with the impaired lung function following acute COVID-19. Single cell transcriptomic analysis identified the potential pathogenic subsets of respiratory CD8+ T cells contributing to persistent tissue conditions following COVID-19. Our results have revealed pathophysiological and immune traits that may support the development of lung sequelae following SARS-CoV-2 pneumonia in older individuals, with implications for the treatment of chronic COVID-19 symptoms."

JAMA Netw Open: [Symptoms and Health Outcomes Among Survivors of COVID-19 Infection 1 Year After Discharge From Hospitals in Wuhan, China](#) (29 September 2021)

"Question: What are the long-term health outcomes associated with COVID-19 infection 1 year after hospital discharge?

Findings: In this cohort study of 2433 patients who had been hospitalized with COVID-19, the most common symptoms at 1 year after discharge were fatigue, sweating, chest tightness, anxiety, and myalgia. Patients with severe disease had more postinfection symptoms and higher chronic obstructive pulmonary disease assessment test scores.

Meaning: This study reported prolonged symptoms of COVID-19 and found that severe disease during hospitalization was a risk factor for more symptoms and higher chronic obstructive pulmonary disease assessment test scores."

Thorax: [Physical, cognitive and mental health outcomes in 1-year survivors of COVID-19-associated ARDS](#) (29 September 2021)

"We report on the outcome of 114 COVID-19-associated acute respiratory distress syndrome (ARDS) survivors evaluated at 3, 6 and 12 months after intensive care unit discharge with assessment of physical, mental and cognitive impairments. Critical illness polyneuromyopathy was diagnosed in 23 patients (39%). Handgrip dynamometry was 70% predicted at 3 months and significantly improved over time, whereas the 6 min walk test (80% predicted) and severe fatigue (27% of patients) did not. Independence in activities of daily living (ADL) was achieved by 98% at 3 months. Cognitive impairment (28% at 3 months) improved over time, whereas depression, anxiety and post-traumatic stress disorder symptoms, present in 9%, 10% and 4% at 3 months, did not. Normalised health-related quality of life was good. COVID-19-associated ARDS leads to persisting impairment in performance-based measures of physical function, while ADL, cognitive and mental health status, and health-related quality of life may be less impaired."

PLoS Med: [Incidence, co-occurrence, and evolution of long-COVID features: A 6-month retrospective cohort study of 273,618 survivors of COVID-19](#) (28 September 2021)

"Why was this study done?"

- Long-COVID has been described in recent studies. But we do not know the risk of developing features of this condition and how it is affected by factors such as age, sex, or severity of infection.
- We do not know if the risk of having features of long-COVID is more likely after Coronavirus Disease 2019 (COVID-19) than after influenza.
- We do not know about the extent to which different features of long-COVID co-occur.

What did the researchers do and find?

- This research used data from electronic health records of 273,618 patients diagnosed with COVID-19 and estimated the risk of having long-COVID features in the 6 months after a diagnosis of COVID-19. It compared the risk of long-COVID features in different groups within the population and also compared the risk to that after influenza.
- The research found that over 1 in 3 patients had one or more features of long-COVID recorded between 3 and 6 months after a diagnosis of COVID-19. This was significantly higher than after influenza.
- For 2 in 5 of the patients who had long-COVID features in the 3- to 6-month period, they had no record of any such feature in the previous 3 months.
- The risk of long-COVID features was higher in patients who had more severe COVID-19 illness, and slightly higher among females and young adults. White and non-white patients were equally affected.

What do these findings mean?

- Knowing the risk of long-COVID features helps in planning the relevant healthcare service provision.
- The fact that the risk is higher after COVID-19 than after influenza suggests that their origin might, in part, directly involve infection with SARS-CoV-2 and is not just a general consequence of viral infection. This might help in developing effective treatments against long-COVID.
- The findings in the subgroups, and the fact that the majority of patients who have features of long-COVID in the 3- to 6-month period already had symptoms in the first 3 months, may help in identifying those at greatest risk."

Women's Health, Pregnancy, and Perinatal Care

News in Brief

The CDC calls for urgent action for COVID-19 vaccines "among people who are pregnant, recently pregnant (including those who are lactating), who are trying to become pregnant now, or who might become pregnant in the future" ([CDC](#)).

Journal Articles

Birth: [Perinatal and postpartum care during the COVID-19 pandemic: A nationwide cohort study](#) (07 October 2021)

"Background: This study aimed to analyze perinatal outcomes and adverse events during the COVID-19 pandemic's first wave to help direct decision making in future waves.

Methods: This study was an epidemiological cohort study analyzing comprehensive birth registry data among all 80 obstetric departments in Austria. Out of 469 771 records, 468 348 were considered eligible, whereof those with preterm delivery, birthweight <500 g, multiple fetuses, fetal malformations and chromosomal anomalies, intrauterine fetal death, maternal cancer, HIV infection, and/or inter-hospital transfers were excluded. Women who delivered between January and June 2020 were then classified as cases, whereas those who delivered between January and June 2015-2019 were classified as controls. Perinatal outcomes, postpartum hospitalization, and adverse events served as outcome measures.

Results: Of 33 198 cases and 188 225 controls, data analysis showed significantly increased rates of labor induction, instrumental delivery, obstetric anesthesia, NICU transfer, and 5-min Apgar score below 7 during the COVID-19 period. There was a significantly shorter

length of postpartum hospitalization during the COVID-19 period compared with the non-COVID-19 period (3.1 ± 1.4 vs 3.5 ± 1.5 days; $P < .001$). Significantly more women opted for short-stay delivery during the COVID-19 period (3.7% vs 2.4%; $P < .001$). Those who delivered during the COVID-19 period were also more likely to experience postpartum adverse events (3.0% vs 2.6%; $P < .001$), which was confirmed in the logistic regression model (odds ratio, 2.137; 95% confidence interval, 1.805-2.530; $P < .001$).

Conclusions: Perinatal and postpartum care during the first wave of the COVID-19 pandemic differed significantly from that provided before. Increased rates of adverse events underline the need to ensure access to high-quality obstetric care to prevent collateral damage."

JAMA Netw Open: [Trends in Infertility Care Among Commercially Insured US Women During the COVID-19 Pandemic](#) (06 October 2021)

"This cross-sectional study uses interrupted time series analysis of administrative claims data to evaluate trends in infertility and assisted reproductive technology utilization rates, including pattern differences by age, income, or race and ethnicity, among commercially insured US women during the COVID-19 pandemic."

Pediatric Population

News in Brief

As of Tuesday, 28 September 2021, Pfizer has submitted data to the FDA for authorization of a lower-dose version of its COVID-19 vaccine for children 5-11 years old ([Pfizer](#)).

In response, FDA's Vaccines and Related Biological Products Advisory Committee is scheduled to meet 26 October 2021 and plans to discuss EUA expansion to include children 5-11 years old at that time ([FDA](#)).

"Some children's hospitals see another surge in rare Covid-19 complication MIS-C" ([CNN](#)).

"How the risk of Covid-19 for kids compares to other dangers — Children are at much lower risk of Covid-19 than adults. But what does that actually mean?" ([Vox](#))

Journal Articles

JAMA Pediatr: [Association of the COVID-19 Pandemic With Routine Childhood Vaccination Rates and Proportion Up to Date With Vaccinations Across 8 US Health Systems in the Vaccine Safety Datalink](#) (07 October 2021)

"Question: Is the COVID-19 pandemic associated with persistent disruptions in routine childhood vaccination in the US, and have there been variations in routine vaccination by age, race, and/or ethnicity?

Findings: In this cohort study using a prepandemic-postpandemic control design with data from 8 US health systems, there were weekly vaccine administration rates that were substantially lower across pediatric age groups during the COVID-19 pandemic. The proportion of participants up to date with vaccinations was lower for the groups aged 7 months, 18 months, and 13 years, while coverage varied by race and ethnicity.

Meaning: Targeted interventions to increase routine childhood vaccination in undervaccinated communities are needed."

Pediatrics: [COVID-19-Associated Orphanhood and Caregiver Death in the United States](#) (07 October 2021)

"Background: Most COVID-19 deaths occur among adults, not children, and attention has focused on mitigating COVID-19 burden among adults. However, a tragic consequence of adult deaths is that high numbers of children might lose their parents and caregivers to COVID-19-associated deaths.

Methods: We quantified COVID-19-associated caregiver loss and orphanhood in the US and for each state using fertility and excess and COVID-19 mortality data. We assessed burden and rates of COVID-19-associated orphanhood and deaths of custodial and co-residing grandparents, overall and by race/ethnicity. We further examined variations in COVID-19-associated orphanhood by race/ethnicity for each state.

Results: We found that from April 1, 2020 through June 30, 2021, over 140,000 children in the US experienced the death of a parent or grandparent caregiver. The risk of such loss was 1.1 to 4.5 times higher among children of racial and ethnic minorities, compared to Non-Hispanic White children. The highest burden of COVID-19-associated death of parents and caregivers occurred in Southern border states for Hispanic children, Southeastern states for Black children, and in states with tribal areas for American Indian/Alaska Native populations.

Conclusions: We found substantial disparities in distributions of COVID-19-associated death of parents and caregivers across racial and ethnic groups. Children losing caregivers to COVID-19 need care and safe, stable, and nurturing families with economic support, quality childcare and evidence-based parenting support programs. There is an urgent need to mount an evidence-based comprehensive response focused on those children at greatest risk, in the states most affected."

JAMA Netw Open: [Association of Children's Physical Activity and Screen Time With Mental Health During the COVID-19 Pandemic](#) (01 October 2021)

"Question: What is the association of children's physical activity and screen time with mental health during the COVID-19 pandemic?

Findings: In this cross-sectional national survey that included 1000 school-aged children in the US, children who engaged in more physical activity and less screen time had better mental health outcomes as measured by the Strengths and Difficulties Questionnaire.

Meaning: These findings suggest that physical activity and screen time may be targets for promoting children's mental health during and after the COVID-19 pandemic."

Pediatrics: [IVIG Compared to IVIG Plus Infliximab in Multisystem Inflammatory Syndrome in Children](#) (21 September 2021)

"Objective: To compare initial treatment with intravenous immunoglobulin (IVIG) to IVIG plus infliximab in multisystem inflammatory syndrome in children (MIS-C).

Methods: Single-center retrospective cohort study of patients with MIS-C who met Centers for Disease Control and Prevention criteria and received treatment from April 2020 through February 2021. Patients were included and compared based on initial therapy of either IVIG alone or IVIG plus infliximab. Primary outcome was need for additional therapy 24 hours or more after treatment initiation.

Results: 72 children with MIS-C met inclusion criteria. Additional therapy was needed in 13/20 (65%) who received IVIG alone and 16/52 (31%) who received IVIG plus infliximab ($P=0.01$). Median (interquartile range) intensive care unit (ICU) length-of-stay was 3.3 (2.2, 3.8) and 1.8 (1.1, 2.1) days, respectively ($P=0.001$).

New or worsened left ventricular dysfunction developed in 4/20 (20%) and 2/52 (4%) ($P=0.05$), and new vasoactive medication requirement developed in 3/20 (15%) and 2/52 (4%), respectively ($P=0.13$). Median percent change in C-reactive protein (CRP) at 24 hours post-treatment compared to pre-treatment level was 0% (-29, 66) and -46% (-62, -15), ($P<0.001$); and at 48 hours post-treatment was -5% (-41, 57) and -70% (-79, -49), respectively ($P<0.001$). There was no significant difference in hospital length-of-stay, time to fever resolution, vasoactive medication duration, or need for diuretics.

Conclusions: Patients with MIS-C treated initially with IVIG plus infliximab compared to IVIG alone were less likely to require additional therapy and had decreased ICU length-of-stay, decreased development of left ventricular dysfunction, and more rapid CRP decline."

Healthcare Workers

News in Brief

"Healthcare workforce bills moving along in Congress — Bill to increase Medicare-funded GME slots gains another Senate co-sponsor" ([Medpage](#)).

Opinion: "I fear Covid-19 is pushing young physicians out of medicine" ([STAT](#)).

"New York hospitals fire, suspend staff who refuse COVID vaccine" ([Reuters](#)).

"A New York healthcare worker who was just fired for refusing the COVID-19 shot says she wouldn't get it even if God said 'you must take this vaccine'" ([Insider](#)).

"The ripple effect of the delta surge — Hospitals in states with fewer COVID-19 cases are fielding transfer requests from across the country, straining hospital resources" ([AAMC](#)).

Opinion: "Covid-19 keeps delivering lessons about health care worker burnout. Will we learn them?" ([STAT](#)).

Journal Articles

Workplace Health Saf: ["We All Held Our Own": Job Demands and Resources at Individual, Leader, Group, and Organizational Levels During COVID-19 Outbreak in Health Care. A Multi-Source Qualitative Study](#) (07 October 2021)

"Background: Interventions tackling COVID-19 impact on health care workers' mental health would benefit from being informed by validated and integrated assessment frameworks. This study aimed to explore the fitness of integrating the Job Demands-Resources (JD-R) model and the Individual-Group-Leader-Organization (IGLO) framework to investigate the pandemic's impact on health care workers' mental health.

Methods: Qualitative data were collected via 21 semi-structured interviews with senior and middle managers and four focus groups with employees (doctors, nurses, health care assistants) from three areas (Department of Emergency, Department of Medicine, Research Institute of Neuroscience) of a large health care institution facing the first wave of COVID-19. NVivo deductive content analysis of text data was performed.

Findings: Several COVID-19-related job demands and resources were found at IGLO levels. Individual-level demands included emotional load, while resources included resilience and motivation. Group-level demands included social distancing, while resources included team support and cohesion. Leader-level demands included managers' workload, while resources included leader support. Organizational-level demands included work reorganization, while resources included mental health initiatives.

Conclusions/application to practice: Integrating JD-R and IGLO proved feasible, as job demands and resources could be categorized according to the individual, group, leader, and organization framework. The findings expand previous studies by filling the lack of knowledge on how job demands and resources might unfold at different workplace levels during a pandemic. Results provide unit-level evidence for designing and implementing multilevel interventions to manage health care workers' mental health during COVID-19 and future pandemics. Our findings offer occupational health practitioners a suitable approach to perform workplace mental health assessment activities."

BMC Psychiatry: [Resilience, coping, and distress among healthcare service personnel during the COVID-19 pandemic](#) (06 October 2021)

"Background: The COVID-19 pandemic has a detrimental effect on the health and well-being of health care workers (HCWs). The extent to which HCWs may differ in their experience of depression and anxiety is unclear, and longitudinal studies are lacking. The present study examined theorized differences in distress between resilient and non-resilient HCWs over time, as reported in a national online survey. We also examined possible differences in distress as a function of sex and doctoral-level status.

Methods: A national sample responded to an online survey data that included the study measures. Of the HCWs who responded, 666 had useable data at the two time points. A longitudinal structural equation model tested an a priori model that specified the relationship of a resilient personality prototype to self-reported resilience, coping, depression and anxiety at both measurement occasions. Additional invariance models examined possible differences by sex and doctoral-level status.

Results: The final model explained 46.4% of the variance in psychological distress at Time 1 and 69.1% at Time 2. A non-resilient personality prototype predicted greater depression and anxiety. A resilient personality prototype was predictive of and operated through self-reported resilience and less disengaged coping to effect lower distress. No effects were found for active coping, however. The final model was generally invariant by sex and HCWs status. Additional analyses revealed that non-doctoral level HCWs had significantly higher depression and anxiety than doctoral-level HCWs on both occasions.

Conclusions: HCWs differ in their susceptibility to distress imposed by COVID-19. Those who are particularly vulnerable may have characteristics that contribute to a lower sense of confidence and efficacy in stressful situations, and more likely to rely on ineffective, disengaged coping behaviors that can exacerbate stress levels. Individual interventions and institutional policies may be implemented to support HCWs at risk."

Clin Infect Dis: [Association between Airborne Infection Isolation Room Utilization Rates and Healthcare Worker COVID-19 Infections in Two Academic Hospitals](#) (02 October 2021)

"We compared healthcare worker SARS-CoV-2 infection rates between March-August 2020 in two similar hospitals with high versus low airborne infection isolation room utilization rates but otherwise identical infection control policies. We found no difference in healthcare worker infection rates between the two hospitals nor between patient-facing vs non-patient-facing providers."

Mental Health, Psychosocial Issues, and Wellness

News in Brief

"What do all these stories of vaccine denial deaths do to our sense of empathy?" ([WP](#))

"CDC struggles to expand pandemic response team as morale plummets" ([Politico](#)).

"Mental health: build predictive models to steer policy — Combine economic, social and medical data to forecast need and design services to address the growing crisis" ([Nature](#)).

"Obesity rates rise during pandemic, fueled by stress, job loss, sedentary lifestyle" ([NPR](#)).

Special Reports and Other Resources

DOD DSPO: [CY 2020 Annual Suicide Report \[pdf\]](#) (30 September 2021)

"Today, the Department of Defense (DOD) released the Calendar Year (CY) 2020 Annual Suicide Report (ASR). We continue to take action to prevent suicides while supporting our military members and their families. Every death by suicide is a tragedy. The CY 2020 ASR presents recent suicide data for Service members and their families, and describes current and future efforts underway to combat suicide....

While suicide rates are not going in the desired direction, the Department did not see a statistical change in suicide rates between CY 2020 and CY 2019 or CY 2018 that would indicate a COVID-19-related increase. We recognize the impact of COVID-19 on the well-being of our force and our Nation. During this time, we continue our efforts to educate and support the force, promote a variety of resources such as mental telehealth resources and financial counseling, and emphasize social connectedness....

In CY 2020, there were 580 Service members who tragically died by suicide. The ASR for CY 2020 shows that the suicide rate for the Active Component statistically increased from CY

2015 to CY 2020. There was no statistically significant increase or decrease for the Reserve and National Guard from CY 2015 to CY 2020. In the near-term for the Reserve, the CY 2020 rate was statistically comparable to both CY 2019 and CY 2018; the National Guard rate had statistically decreased from CY 2018 to CY 2019, returning to a comparable level in CY 2020....

Based on the findings from this year's report, the Department will focus on addressing perceived barriers to seeking help and encourage use of support resources, especially among young and enlisted members. For example, the Department is expanding a promising help-seeking focused training pilot to geographically-isolated Service members and those outside the continental United States.

For military families, the Department is increasing screening of military families for depression and suicide risk, supporting an outreach campaign to normalize relationship help-seeking, and expanding safety and safe storage of lethal means, such as firearms and medications. The Department is also exploring ways to better understand help-seeking behaviors, perceived barriers to care, and suicide thoughts and behaviors among military spouses.

The CY 2020 report includes Fiscal Year 2020/2021 National Defense Authorization Act reporting requirements, and represents the department's continued commitment to provide transparency, accountability, and timely information on this critical issue."

(text taken from [DOD news release](#))

Journal Articles

MMWR: [National and State Trends in Anxiety and Depression Severity Scores Among Adults During the COVID-19 Pandemic — United States, 2020–2021](#) (08 October 2021)

"What is already known about this topic? U.S. Census Bureau Household Pulse Survey data indicate that the percentage of U.S. adults with symptoms of anxiety and depressive disorders increased nationwide from August 2020 to February 2021.

What is added by this report? Nationwide, average anxiety severity scores increased 13% from August to December 2020 and then decreased 26.8% from December 2020 to June 2021. Similar increases and decreases occurred in depression severity scores.

What are the implications for public health practice? Mental health services and resources, including telehealth behavioral services, are critical during the COVID-19 pandemic."

Lancet Reg Health Am: [Persistent depressive symptoms during COVID-19: a national, population-representative, longitudinal study of U.S. adults](#) (04 October 2021)

"Background: The COVID-19 pandemic and its consequences have been associated with an increase in poor population mental health. We assessed how depressive symptoms changed among U.S. adults over the course of the COVID-19 pandemic and identified the key risk factors for these symptoms.

Methods: Longitudinal panel study of a nationally representative group of U.S. adults ages 18 years and older surveyed in March-April 2020 (Time 1; N=1441) and March-April 2021 (Time 2; N=1161) in the COVID-19 and Life Stressors Impact on Mental Health and Well-being study (CLIMB). The Patient Health Questionnaire-9 (PHQ-9) was used to define elevated depressive symptoms (cut-off ≥ 10) and depressive symptoms score (0-27).

Findings: The prevalence of elevated depressive symptoms persisted from 27.8% in 2020 (95% CI: 24.9, 30.9) to 32.8% in 2021 (95% CI: 29.1, 36.8). Over time, the central drivers of depressive symptoms were low household income, not being married, and experiencing multiple stressors during the COVID-19 pandemic. The odds ratio of elevated depressive symptoms for low income relative to high income persons increased from 2.3 (95% CI: 1.2, 4.2) in 2020 to 7.0 (95% CI: 3.7, 13.3) in 2021. Fewer people reported experiencing 4 or more COVID-19 stressors in 2021 than in 2020 (47.5% in 2020 vs 37.1% in 2021), but the odds ratio of elevated depressive symptoms associated with 4 or more stressors relative to 1 stressor or less increased from 1.9 (95% CI: 1.2, 3.1) in 2020 to 5.4 (95% CI: 3.2, 9.2) in 2021.

Interpretation: The burden of depressive symptoms in the U.S. adult population increased over the course of the COVID-19 pandemic. Mental health gaps grew between populations with different assets and stressor experiences during the COVID-19 pandemic."

Autism Res: [The impact of COVID-19 on the mental health and wellbeing of caregivers of autistic children and youth: A scoping review](#) (30 September 2021)

"Caregivers and families of autistic people have experienced stress and increase in demands due to the COVID-19 pandemic that may have long-term negative consequences for both their own and their children's mental health. A scoping review was conducted to identify pandemic related demands experienced by caregivers and families of autistic children and youth. The review also consolidated information on coping strategies and parenting-related guidelines that have emerged to help parents meet these demands. Search strategies were approved by a research librarian and were conducted in peer-reviewed and gray literature databases between May 2020 and February 2021. Additional resources were solicited through author networks and social media. All articles were published between December 2019 and February 2021. Article summaries were charted, and a thematic analysis was conducted with confirmation of findings with our knowledge users. Twenty-three published

articles and 14 pieces of gray literature were included in the review. The majority of articles characterized and highlighted the increase in demands on caregivers of autistic children and youth during the pandemic globally. Both quantitative and qualitative studies suggest that parents have experienced an increase in stress and mental health-related symptoms during lockdown measures. Findings suggest that families are employing coping strategies, but there no evidence-based supports were identified. The review highlighted the potential long-term impact of prolonged exposure to increasing demands on the mental health and wellbeing of caregivers and families of autistic people, and pointed to a need for the rapid development and evaluation of flexible and timely support programs."

Br J Psychiatr: [Pre-pandemic mental health and disruptions to healthcare, economic and housing outcomes during the COVID-19 pandemic: evidence from 12 UK longitudinal studies](#) (30 September 2021)

"Background: The COVID-19 pandemic has disrupted lives and livelihoods, and people already experiencing mental ill health may have been especially vulnerable.

Aims: Quantify mental health inequalities in disruptions to healthcare, economic activity and housing.

Method: We examined data from 59 482 participants in 12 UK longitudinal studies with data collected before and during the COVID-19 pandemic. Within each study, we estimated the association between psychological distress assessed pre-pandemic and disruptions since the start of the pandemic to healthcare (medication access, procedures or appointments), economic activity (employment, income or working hours) and housing (change of address or household composition). Estimates were pooled across studies.

Results: Across the analysed data-sets, 28% to 77% of participants experienced at least one disruption, with 2.3–33.2% experiencing disruptions in two or more domains. We found 1 s.d. higher pre-pandemic psychological distress was associated with (a) increased odds of any healthcare disruptions (odds ratio (OR) 1.30, 95% CI 1.20–1.40), with fully adjusted odds ratios ranging from 1.24 (95% CI 1.09–1.41) for disruption to procedures to 1.33 (95% CI 1.20–1.49) for disruptions to prescriptions or medication access; (b) loss of employment (odds ratio 1.13, 95% CI 1.06–1.21) and income (OR 1.12, 95% CI 1.06 –1.19), and reductions in working hours/furlough (odds ratio 1.05, 95% CI 1.00–1.09) and (c) increased likelihood of experiencing a disruption in at least two domains (OR 1.25, 95% CI 1.18–1.32) or in one domain (OR 1.11, 95% CI 1.07–1.16), relative to no disruption. There were no associations with housing disruptions (OR 1.00, 95% CI 0.97–1.03).

Conclusions: People experiencing psychological distress pre-pandemic were more likely to experience healthcare and economic disruptions, and clusters of disruptions across multiple domains during the pandemic. Failing to address these disruptions risks further widening mental health inequalities."

Disparities and Health Equity

News in Brief

"Covid is killing rural Americans at twice the rate of urbanites" ([KHN](#)).

Long read: "At a rural ICU, Covid-19's summer surge put telehealth to the test" ([STAT](#)).

Special Reports and Other Resources

GAO: [Health Care Capsule: Racial and Ethnic Health Disparities](#) (23 September 2021)

"People from various racial and ethnic groups may experience health disparities—preventable differences in health outcomes. Discrimination, economic instability, and lack of health care access are some of the factors that can contribute to these disparities.

Our 2-page 'capsule' draws from several GAO reports to provide examples of these health disparities, such as COVID-19, maternal mortality, chronic health conditions, as well as disparities among veterans. We also offer policy considerations to help the federal government better understand health disparities and promote health equity."

Journal Articles

JAMA Netw Open: [Evaluation of Racial, Ethnic, and Socioeconomic Disparities in Initiation of Kidney Failure Treatment During the First 4 Months of the COVID-19 Pandemic](#) (07 October 2021)

"Question: How did the volume and characteristics of patients initiating treatment for incident kidney failure change early in the COVID-19 pandemic, and were these changes associated with race, ethnicity, or socioeconomic status?

Findings: In this cross-sectional study of 127 149 US adults with incident kidney failure during the first 4 months of the pandemic (March 1 through June 30, 2020), the number of patients initiating treatment for incident kidney failure declined by 30%, with Black patients and patients living in counties with high COVID-19 mortality initiating treatment with significantly worse levels of kidney function when compared with prior years.

Meaning: These results suggest that declines in the number of patients with incident kidney failure may indicate delayed treatment initiation or changes in care delivery during the pandemic."

Ann Intern Med: [Racial and Ethnic Disparities in Excess Deaths During the COVID-19 Pandemic, March to December 2020](#) (05 October 2021)

"Background: Although racial/ethnic disparities in U.S. COVID-19 death rates are striking, focusing on COVID-19 deaths alone may underestimate the true effect of the pandemic on disparities. Excess death estimates capture deaths both directly and indirectly caused by COVID-19.

Measurements: Excess deaths and excess deaths per 100 000 persons from March to December 2020 were estimated by race/ethnicity, sex, age group, and cause of death, using provisional death certificate data from the Centers for Disease Control and Prevention (CDC) and U.S. Census Bureau population estimates.

Results: An estimated 2.88 million deaths occurred between March and December 2020. Compared with the number of expected deaths based on 2019 data, 477 200 excess deaths occurred during this period, with 74% attributed to COVID-19. Age-standardized excess deaths per 100 000 persons among Black, American Indian/Alaska Native (AI/AN), and Latino males and females were more than double those in White and Asian males and females. Non-COVID-19 excess deaths also disproportionately affected Black, AI/AN, and Latino persons. Compared with White males and females, non-COVID-19 excess deaths per 100 000 persons were 2 to 4 times higher in Black, AI/AN, and Latino males and females, including deaths due to diabetes, heart disease, cerebrovascular disease, and Alzheimer disease. Excess deaths in 2020 resulted in substantial widening of racial/ethnic disparities in all-cause mortality from 2019 to 2020.

Conclusion: There were profound racial/ethnic disparities in excess deaths in the United States in 2020 during the COVID-19 pandemic, resulting in rapid increases in racial/ethnic disparities in all-cause mortality between 2019 and 2020."

MMWR: [Disparities in COVID-19 Vaccination Status, Intent, and Perceived Access for Noninstitutionalized Adults, by Disability Status — National Immunization Survey Adult COVID Module, United States, May 30–June 26, 2021](#) (01 October 2021)

"What is already known about this topic? Persons with disabilities are at increased risk for COVID-19–related illness and death.

What is added by this report? Analysis of the National Immunization Survey Adult COVID Module found that, compared with adults without a disability, those with a disability had a lower likelihood of having received COVID-19 vaccination, despite being less likely to report hesitancy about getting vaccinated. Adults with a disability reported more difficulties obtaining a COVID-19 vaccine than did persons without a disability.

What are the implications for public health practice? Reducing barriers to scheduling and making vaccination sites more accessible might improve vaccination coverage among persons with disabilities."

JAMA Netw Open: [Disparities and Temporal Trends in COVID-19 Exposures and Mitigating Behaviors Among Black and Hispanic Adults in an Urban Setting](#) (28 September 2021)

"Question: What behaviors and disparities in health resources are associated with the spread of COVID-19 in predominantly Black and Hispanic communities?

Findings: In this survey study of adults living in a large US city, consistent masking was associated with a decrease in SARS-CoV-2 acquisition; however, Hispanic individuals were at higher risk for infection, more often worked outside the home, and were less likely to have received economic aid through stimulus checks or unemployment benefits.

Meaning: These results suggest public health messaging may have improved preventive behaviors over time but should be customized for Hispanic communities."

JAMA Health Forum: Health Forum: [Confronting Anti-Asian Racism and Health Disparities in the Era of COVID-19](#) (24 September 2021)

"This Viewpoint confronts the anti-Asian racism and health disparities that have been revealed during the challenges of the COVID-19 pandemic."

PLOS One: [Census tract socioeconomic indicators and COVID-19-associated hospitalization rates—COVID-NET surveillance areas in 14 states, March 1–April 30, 2020](#) (24 September 2021)

"Objectives: Some studies suggested more COVID-19-associated hospitalizations among racial and ethnic minorities. To inform public health practice, the COVID-19-associated Hospitalization Surveillance Network (COVID-NET) quantified associations between race/ethnicity, census tract socioeconomic indicators, and COVID-19-associated hospitalization rates.

Methods: Using data from COVID-NET population-based surveillance reported during March 1-April 30, 2020 along with socioeconomic and denominator data from the US Census Bureau, we calculated COVID-19-associated hospitalization rates by racial/ethnic and census tract-level socioeconomic strata.

Results: Among 16,000 COVID-19-associated hospitalizations, 34.8% occurred among non-Hispanic White (White) persons, 36.3% among non-Hispanic Black (Black) persons, and 18.2% among Hispanic or Latino (Hispanic) persons. Age-adjusted COVID-19-associated hospitalization rate were 151.6 (95% Confidence Interval (CI): 147.1-156.1) in census tracts with >15.2%-83.2% of persons living below the federal poverty level (high-poverty census tracts) and 75.5 (95% CI: 72.9-78.1) in census tracts with 0%-4.9% of persons living below the federal poverty level (low-poverty census tracts). Among White, Black, and Hispanic

persons living in high-poverty census tracts, age-adjusted hospitalization rates were 120.3 (95% CI: 112.3-128.2), 252.2 (95% CI: 241.4-263.0), and 341.1 (95% CI: 317.3-365.0), respectively, compared with 58.2 (95% CI: 55.4-61.1), 304.0 (95% CI: 282.4-325.6), and 540.3 (95% CI: 477.0-603.6), respectively, in low-poverty census tracts.

Conclusions: Overall, COVID-19-associated hospitalization rates were highest in high-poverty census tracts, but rates among Black and Hispanic persons were high regardless of poverty level. Public health practitioners must ensure mitigation measures and vaccination campaigns address needs of racial/ethnic minority groups and people living in high-poverty census tracts."

JAMA Ophthalmol: [Association of Patient Characteristics With Delivery of Ophthalmic Telemedicine During the COVID-19 Pandemic](#) (23 September 2021)

"Question: During the first year of the COVID-19 pandemic in the US, were there differences in the characteristics of patients who received ophthalmic care via telemedicine compared with in-person care?

Findings: In this cross-sectional study of 1911 patients from a single academic ophthalmology practice, patients who were men, self-identified as Black, did not speak English, had an educational level of high school or less, and were of older age were less likely to receive telemedical care compared with in-person care.

Meaning: These results suggest that disparities in the delivery of ophthalmic telemedical care existed during the COVID-19 pandemic and support prioritizing health equity in future telemedicine programs."

Risk, Transmission, and Exposure

News in Brief

A new study points to the power of wearables to predict even presymptomatic infections, suggesting use one day against Covid-19" ([STAT](#); see also: [JAMA Netw Open article](#)).

"Why are Americans still—still!—wearing cloth masks? It's long past time for an upgrade" ([Atlantic](#)).

"Real-world data show that filters clean COVID-causing virus from air" ([Nature](#)).

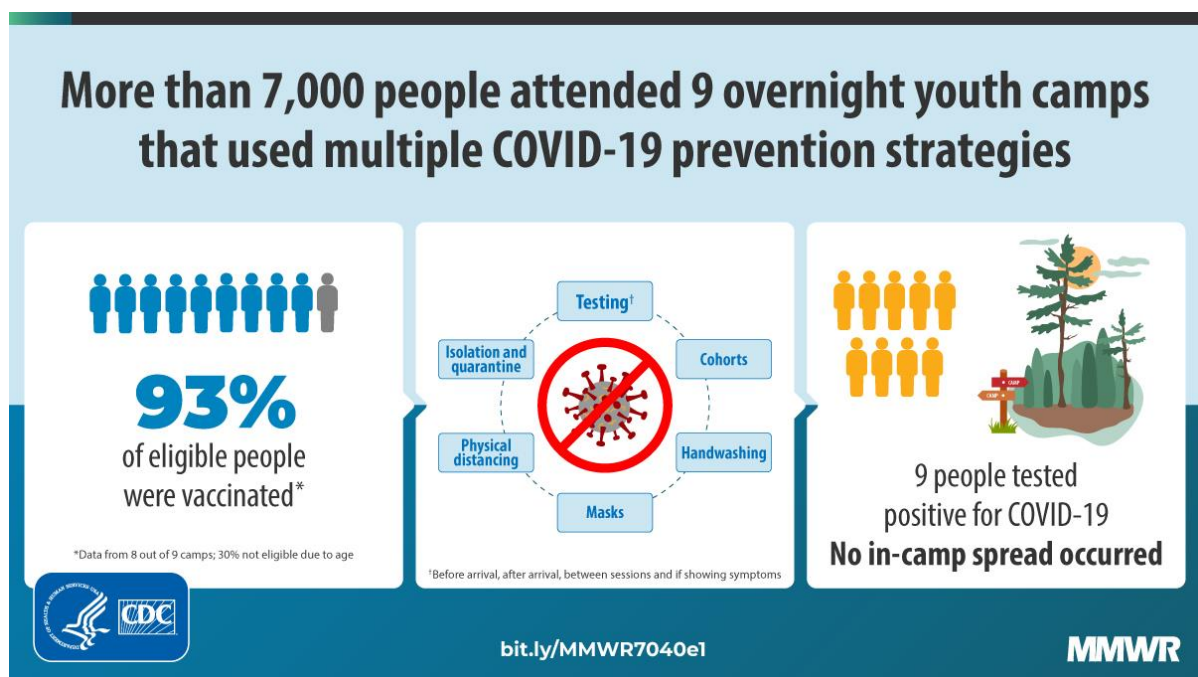
Special Reports and Other Resources

JHCHS: [Masks and Respirators for the 21st Century: Policy Changes Needed to Save Lives and Prevent Societal Disruption](#) (05 October 2021)

"In this report, we provide an overview of the history and types of masks and respirators that exist and consider the development, manufacture, approval, and stockpiling of better respiratory protection for healthcare workers, the nonhealthcare workforce, and the public in the United States. We address issues related to acceptance and willingness to wear face coverings, masks, or respirators. We discuss ways to foster ingenuity in designs of new devices, promote advanced development, obtain regulatory approval, and stockpile a reasonable number of devices."

Journal Articles

MMWR: [Multicomponent Strategies to Prevent SARS-CoV-2 Transmission — Nine Overnight Youth Summer Camps, United States, June–August 2021](#) (08 October 2021)



"What is already known about this topic? Previous studies have demonstrated the importance of prevention strategies to reduce SARS-CoV-2 transmission in overnight camps.

What is added by this report? During June–August 2021, a total of 7,173 campers and staff members attended nine U.S. overnight camps that implemented multiple prevention strategies including high vaccination coverage (>93% among eligible persons aged ≥12 years); prearrival and frequent screening testing (38,059 tests); and additional concomitant

prevention measures. Nine laboratory-confirmed COVID-19 cases and no secondary infections were detected.

What are the implications for public health practice? Implementation of high vaccination coverage coupled with multiple prevention strategies is critical to averting COVID-19 outbreaks in congregate settings, including overnight camps. These findings highlight important guiding principles for school and youth-based COVID-19 prevention protocols."

PLoS Med: [Predictive symptoms for COVID-19 in the community: REACT-1 study of over 1 million people](#) (28 September 2021)

"Why was this study done?

- The rapid detection of SARS-CoV-2 infection in the community is key to ensuring efficient control of transmission via isolation.
- Eligibility for community PCR testing is determined based on the reported presence of several (predetermined) symptoms, which may vary from one country to another.
- Quantitative evidence measuring which symptoms are the most informative of a COVID-19 infection remains scarce.

What did the researchers do and find?

- Data were collected from over 1 million participants in the REACT-1 study (June 2020 to January 2021), for whom 26 symptoms were assayed and the results of a PCR test were available.
- Adopting a variable selection approach, we sought to determine the best combination of symptoms jointly and complementarily predictive of PCR positivity and investigated whether these symptoms were the same between individuals infected by the wild-type virus and those infected by the B.1.1.7 variant.
- We identified 7 symptoms that were jointly predictive of PCR positivity and appeared to vary only marginally across age groups: loss or change of sense of smell, loss or change of sense of taste, fever, new persistent cough, chills, appetite loss, and muscle aches.
- These symptoms were also predictive of the B.1.1.7 infection, together with sore throat (to a lesser extent).

What do these findings mean?

- Taken together, these 7 symptoms can improve the detection of COVID-19 infection in the community.
- Using this sparse set of symptoms for test allocation would increase the number of tests performed (up to 30%–40% of symptomatic individuals being tested) but would enable up to 75% of symptomatic cases to be detected.

- This set of 7 symptoms is also predictive of B.1.1.7 infection and performs similarly across age groups. Its use would maximize the case detection rate in the community and would be particularly relevant in situations where test capacity is limited."

Disaster Med Public Health Prep: [Occupational Health and Safety Measures in Healthcare Settings During COVID-19: Strategies for Protecting Staff, Patients and Visitors](#) (14 September 2021)

"The COVID-19 (SARS-CoV-2) pandemic has profoundly impacted almost every aspect of healthcare systems worldwide, placing the health and safety of frontline healthcare workers at risk and still continues to remain an important public health challenge. Several hospitals have put in place strategies to manage space, staff, and supplies in order to continue to deliver optimum care to patients while at the same time protecting the health and safety of staff and patients. However, the emergence of the second and third waves of the virus with the influx of new cases continue to add an additional level of complexity to the already challenging situation of containing the spread and lowering the rate of transmission and thus pushing healthcare systems to the limit. In this narrative review paper we describe various strategies including administrative controls, environmental controls and use of personal protective equipment implemented by occupational health and safety departments for the protection of healthcare workers, patients and visitors from SARS-CoV-2 virus infection. The protection and safeguard of the health and safety of healthcare workers and patients through the implementation of effective infection control measures, adequate management of possible outbreaks and minimization of risk of nosocomial transmission is an important and effective strategy of SARS-CoV-2 pandemic management in any healthcare facility. High quality patient care hinges on ensuring that the care providers are well protected and supported so they can provide the best quality of care to their patients."

Health Messaging and Misinformation

News in Brief

"'Vigilante treatments': Anti-vaccine groups push people to leave ICUs. As the anti-vaccine movement escalates its rhetoric, doctors warn that they're dealing with the fallout: 'They're starting to target people, the messengers — nurses and doctors'" ([NBC](#)).

"YouTube is banning prominent anti-vaccine activists and blocking all anti-vaccine content" ([WP](#)).

"Doctors grow frustrated over COVID-19 denial, misinformation" ([AP](#)).

Opinion: "Examining the underpinnings of COVID anti-vaccine sentiment — Public health messaging has fallen short thus far; it's time for a new approach" ([Medpage](#)).

Journal Articles

Big Data Soc: [Different types of COVID-19 misinformation have different emotional valence on Twitter](#) (22 September 2021)

"The spreading of COVID-19 misinformation on social media could have severe consequences on people's behavior. In this paper, we investigated the emotional expression of misinformation related to the COVID-19 crisis on Twitter and whether emotional valence differed depending on the type of misinformation.

We collected 17,463,220 English tweets with 76 COVID-19-related hashtags for March 2020. Using Google Fact Check Explorer API we identified 226 unique COVID-19 false stories for March 2020. These were clustered into six types of misinformation (cures, virus, vaccine, politics, conspiracy theories, and other). Applying the 226 classifiers to the Twitter sample we identified 690,004 tweets. Instead of running the sentiment on all tweets we manually coded a random subset of 100 tweets for each classifier to increase the validity, reducing the dataset to 2,097 tweets.

We found that only a minor part of the entire dataset was related to misinformation. Also, misinformation in general does not lean towards a certain emotional valence. However, looking at comparisons of emotional valence for different types of misinformation uncovered that misinformation related to "virus" and "conspiracy" had a more negative valence than "cures," "vaccine," "politics," and "other." Knowing from existing studies that negative misinformation spreads faster, this demonstrates that filtering for misinformation type is fruitful and indicates that a focus on "virus" and "conspiracy" could be one strategy in combating misinformation. As emotional contexts affect misinformation spreading, the knowledge about emotional valence for different types of misinformation will help to better understand the spreading and consequences of misinformation."

Other Infectious Diseases and Public Health Issues

News in Brief

"Why the WHO approval of the first malaria vaccine is a big deal — Vaccinating against malaria has posed a real challenge for scientists for decades. But the tide may be turning" ([Vox](#); see also: [WHO announcement](#)).

"After 25 years in the dark, the CDC wants to study the true toll of guns in America" ([NPR](#)).

Brazil and the US have confirmed cases of measles ([ONT](#)).

"A man died from rabies in Illinois. Here's why that's so unusual in the U.S." ([NPR](#)).

"West Nile virus deaths rise to 14 in Arizona" ([ONT](#)).

"First drug for dengue, an excruciating disease, may be on the horizon" ([Science](#)).

"*C. difficile* is everywhere – even on the bottom of footwear" ([IDWeek](#)).

"New data shows COVID-19 combined with funding shortfalls are devastating efforts to end TB by 2030 — Less than half of required funding has been provided globally with dramatic consequences as hundreds of thousands more die from TB" ([StopTB](#)).

"The [CDC] is providing a funding mechanism to assist emergency departments in their role as provider-based sentinel networks as part of the Emerging Infections Sentinel Networks (EISN) program" ([Global Biodefense](#)).

"With positive data on mRNA Covid vaccine, Sanofi sets its sights on other pathogens" ([STAT](#)).

Journal Articles

Emerg Infect Dis: [Human Melioidosis Caused by Novel Transmission of *Burkholderia pseudomallei* from Freshwater Home Aquarium, United States](#) (27 September 2021)

"Nearly all cases of melioidosis in the continental United States are related to international travel to areas to which *Burkholderia pseudomallei*, the bacterium that causes melioidosis, is endemic. We report the diagnosis and clinical course of melioidosis in a patient from the United States who had no international travel history and the public health investigation to determine the source of exposure.

We tested environmental samples collected from the patient's home for *B. pseudomallei* by PCR and culture. Whole-genome sequencing was conducted on PCR-positive environmental samples, and results were compared with sequences from the patient's clinical specimen. Three PCR-positive environmental samples, all collected from a freshwater home aquarium that had contained imported tropical fish, were a genetic match to the clinical isolate from the patient. This finding suggests a novel route of exposure and a potential for importation of *B. pseudomallei*, a select agent, into the United States from disease-endemic areas."

Int J Infect Dis: [Post-exposure prophylaxis following high-risk contact with Ebola virus, using immunotherapies with monoclonal antibodies, in the eastern DRC: an emergency use program](#) (26 September 2021)

"Introduction: With the development of therapeutics and vaccine against Ebola Virus Disease, the question of post exposure prophylaxis for high risk contact emerged. Immunotherapies (monoclonal antibodies, mAbs) recently validated for treatment of infected patients appears to be good candidate to protect contacts.

Design: During the 10th EVD outbreak in the Democratic Republic of the Congo, we have administrated mAbs (Mab114 or REGN-EB3) to high and intermediate risk contact of Ebola Virus Disease patients.

Results: Overall, 23 non vaccinated contacts received mAbs after a median delay between contact and post exposure prophylaxis of 1 day (IQR 1,2). 14 days after the contact, all contacts were free of symptoms and all had negative RT-PCR CONCLUSION: Immunotherapies appears to be promising candidates to protect contacts of Ebola Virus Disease. Interaction with vaccine and larger study on efficacy need to be conducted."

MMWR: [Decreased Incidence of Infections Caused by Pathogens Transmitted Commonly Through Food During the COVID-19 Pandemic — Foodborne Diseases Active Surveillance Network, 10 U.S. Sites, 2017–2020](#) (24 September 2021)

"What is already known about this topic? Before 2020, the incidence of infections transmitted commonly by food had not declined for many years.

What is added by this report? During 2020, FoodNet identified 26% fewer infections compared with the average annual number during 2017–2019, including decreased infections associated with international travel.

What are the implications for public health practice? The pandemic and resulting public health response present challenges to explaining changes in observed foodborne illness incidences. Continued surveillance might help elucidate the impact of the COVID-19 pandemic on foodborne illness and identify strategies to decrease illnesses. Concerted efforts are needed to reduce the incidence of these infections from farm to processing plant to restaurants and homes. Consumers can reduce their risk of foodborne illness by following safe food-handling and preparation recommendations."

Statistics

	<i>Total Cases</i>	<i>Total Deaths</i>	<i>Total Vaccine Doses Administered</i>
<i>Global</i>	236,894,900	4,837,041	6,417,886,934
<i>United States</i>	44,160,916	710,189	398,057,328

[JHU CSSE](#) as of 1000 EDT 08 October 2021

<i>Virginia</i>	Total cases (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	888,159	27,861	14,554	19,864	23,629	12,213	10,518	48,362
Hospitalizations	37,264	1,261	647	753	1,465	874	667	2,520
Deaths	13,075	342	219	583	315	228	223	510

[VA DOH](#) as of 1000 EDT 08 October 2021

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